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Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: KHATO SHAHAN-SHAH Examiner #: 78526 Date: 7/20/01
 Art Unit: 1645 Phone Number 30 8-8896 Serial Number: 09610034
 Mail Box and Bldg/Room Location: 8D-17 Results Format Preferred (circle): PAPER DISK E-MAIL
8E-12

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: see attached R/L sheet

Inventors (please provide full names): see attached sheet

Earliest Priority Filing Date: 1/13/98

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Point of Contact:
 Beverly Shears
 Technical Info. Specialist
 CM1 12C14 Tel: 308-4994

Please send elected

claims 1-10 and

35-38

attached
 claims + abstract

Please Rush
 Amended case

A. F. Smith, SPE
 Art Unit 1645
 7/23/01

STAFF USE ONLY

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: <u>Beverly 4994</u>	NA Sequence (#) _____	STN <u>✓</u>
Searcher Phone #: _____	AA Sequence (#) _____	Dialog _____
Searcher Location: _____	Structure (#) _____	Questel/Orbit _____
Date Searcher Picked Up: _____	Bibliographic _____	Dr. Link _____
Date Completed: <u>07-25-01</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: <u>12</u>	Fulltext _____	Sequence Systems _____
Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time: <u>6</u>	Other _____	Other (specify) _____

09/610034

(FILE 'CAPLUS' ENTERED AT 11:47:41 ON 25 JUL 2001)

L1 1231 SEA ABB=ON PLU=ON (MORAXELL? OR M OR BRANHAM? OR
B) (3A) CATARRH?
L2 14 SEA ABB=ON PLU=ON L1 AND (LOS(S) (LIPOOLIGO? OR LIPO
OLIGO?) OR LIPOOLIGOSACCHARID? OR LIPO(W) (OLIGOSACCHARID?
OR OLIGO SACCHARID?) OR LIPOOLIGO SACCHARID?)

L2 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:215844 CAPLUS

DOCUMENT NUMBER: 134:294257

TITLE: Functional characteristics of a protective
monoclonal antibody against serotype A and C
lipooligosaccharides from
Moraxella catarrhalisAUTHOR(S): Hu, Wei-Gang; Chen, Jing; McMichael, John C.;
Gu, Xin-XingCORPORATE SOURCE: Laboratory of Immunology, National Institute on
Deafness and Other Communication Disorders,
Rockville, MD, 20850, USASOURCE: Infect. Immun. (2001), 69(3), 1358-1363
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A monoclonal antibody (MAB), designated MAb 8E7 (IgG3), specific for
Moraxella catarrhalis lipooligosaccharide
(LOS) was evaluated for its functional activity in vitro
and in a mouse model of colonization. ELISA demonstrated that the
MAb 8E7 could be prepd. to a high titer against LOS of the
homologous strain 035E, and that it had bactericidal activity. MAb
8E7 reacted with **M. catarrhalis** serotype A and C
LOSs but not serotype B LOS, as measured by ELISA and Western
blotting. On the basis of published structures of LOSs, this
suggests that the epitope recognized by MAb 8E7 is directed to a
common sequence of either .alpha.-GlcNAc-(1.fwdarw.2)-.beta.-Glc-
(1.fwdarw.at the branch substituting position 4 of the
trisubstituted Glc residue or a terminal tetrasaccharide
.alpha.-Gal-(1.fwdarw.4)-.beta.-Gal-(1.fwdarw.4)-.alpha.-Glc-
(1.fwdarw.2)-.beta.-Glc-(1.fwdarw.at the branch substituting
position 6 of the trisubstituted Glc residue. In a whole-cell
ELISA, MAb 8E7 reacted with 70% of the 30 wild-type strains and
clin. isolates tested. Immuno-electron microscopy demonstrated that
MAb 8E7 reacted with a cell surface-exposed epitope of LOS on strain
035E. MAb 8E7 inhibited the adherence of strain 035E to Chang
conjunctival epithelial cells by 90%. Passive immunization with MAb
8E7 could significantly enhance the clearance of strain 035E from
mouse lungs in an aerosol challenge mouse model. This enhanced
bacterial clearance was inhibited when MAb 8E7 was absorbed by

M. catarrhalis serotype A LOS, indicating that the **M. catarrhalis** LOS-directed antibody may play a major role in the enhancement of **M. catarrhalis** clearance from lungs. These data suggest that MAb 8E7, which recognizes surface-exposed LOS of **M. catarrhalis**, is a protective antibody against **M. catarrhalis**

REFERENCE COUNT: 36
 REFERENCE(S): (1) Ahmed, K; Microb Pathog 2000, V28, P203
 CAPLUS
 (2) Alfa, M; Microb Pathog 1997, V22, P39 CAPLUS
 (3) Barenkamp, S; Infect Immun 1992, V60, P1302
 CAPLUS
 (6) DeMaria, T; Infect Immun 1997, V65, P4431
 CAPLUS
 (8) Edebrink, P; Carbohydr Res 1994, V257, P269
 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2001 ACS
 ACCESSION NUMBER: 2001:23521 CAPLUS
 TITLE: Vaccines for **Moraxella catarrhalis**
 AUTHOR(S): McMichael, J. C.
 CORPORATE SOURCE: Wyeth-Lederle Vaccines, West Henrietta, NY,
 14586-9728, USA
 SOURCE: Vaccine (2000), 19(Suppl. 1), S101-S107
 CODEN: VACCDE; ISSN: 0264-410X
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Vaccine development for **Moraxella catarrhalis** is in the antigen identification stage. **M. catarrhalis** does not appear to synthesize secreted antigens such as exotoxins, nor does it appear to possess a carbohydrate capsule. Modified forms of these antigens are usually good vaccine components. There is some interest in whole bacterial cells and membrane fractions, but the search has largely focused on purified outer surface antigens. All of the present antigens have been selected based on the response seen in animals, although the antibody response seen in people exposed to the bacterium provides some guidance. The antibody response provides information related to the cross-strain preservation of epitopes and whether they are surface exposed. Antigens that elicit antibodies that have complement dependent bactericidal capacity, opsonophagocytic activity or interfere with one of the antigen's known functions such as adhesion or nutrient acquisition are particularly valued. In addn. to examg. the antibody response, some antigens have been

evaluated in a murine pulmonary clearance model. Using these assays and model, several vaccine candidates have been identified. The antigens may be roughly classified by the function they serve the bacterium. One set appears to promote adhesion to host tissues and includes the hemagglutinins, ubiquitous surface protein A1 (UspA1), and possibly the CD protein. A second set is involved in nutrient acquisition. This set includes the lactoferrin binding protein A (LbpA) and lactoferrin binding protein B (LbpB), the transferrin binding protein A (TbpA) and transferrin binding protein B (TbpB), the CD and E porins, and the *Catarrhalis* outer membrane protein B (CopB). A third set is comprised of antigens involved in virulence and it includes lipooligosaccharide (LOS) and the ubiquitous surface protein A2 (UspA2).

Antigens of unknown function, such as the 200K protein, may also be vaccine candidates. The antigens that are most suitable will be detd. in clin. studies that are only beginning now.

REFERENCE COUNT:

53

REFERENCE(S):

- (1) Aebi, C; Infect Immun 1996, V64, P2024
CAPLUS
- (2) Aebi, C; Infect Immun 1997, V65, P4367
CAPLUS
- (3) Aebi, C; Infect Immun 1998, V66, P3113
CAPLUS
- (4) Aebi, C; Infect Immun 1998, V66, P540 CAPLUS
- (5) Ahmed, K; Microbiol Immunol 1991, V35, P361
CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:603738 CAPLUS

DOCUMENT NUMBER: 133:308783

TITLE: Lipooligosaccharide Pk
(Gal.alpha.1-4Gal.beta.1-4Glc) epitope of
Moraxella catarrhalis is a
factor in resistance to bactericidal activity
mediated by normal human serum

AUTHOR(S): Zaleski, Anthony; Scheffler, N. Karoline;
Densen, Peter; Lee, Frank K. N.; Campagnari,
Anthony A.; Gibson, Bradford W.; Apicella,
Michael A.

CORPORATE SOURCE: Department of Microbiology, The University of
Iowa, Iowa City, IA, 52242, USA

SOURCE: Infect. Immun. (2000), 68(9), 5261-5268
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB *Moraxella catarrhalis* is a respiratory pathogen

responsible for acute bacterial otitis media in children and exacerbation of chronic bronchitis in adults. *M. catarrhalis* strains are frequently resistant to the bactericidal activity of normal human serum. In order to det. if the lipooligosaccharide (LOS) of *M. catarrhalis* has a role in serum resistance, the UDP-glucose-4-epimerase (gale) gene was identified, cloned, and sequenced and a deletion/insertion mutation was introduced into *M. catarrhalis* strain 2951. Gale enzymic activity, measured in whole-cell lysates, was ablated in *M. catarrhalis* 2951 gale. Mass spectrometric anal. of LOS isolated with hot phenol-water confirmed that strain 2951 produced a type A LOS. These studies showed that the LOS from 2951 gale had lost two hexose residues due to the gale mutation and that the resultant LOS structure lacked the (Gal.alpha.1-4Gal.beta.1-4Glc) Pk epitope found on *M. catarrhalis* 2951. Wild-type *M. catarrhalis* 2951 is resistant to complement-mediated serum bactericidal activity. In contrast, a greater than 2-log₁₀-unit redn. in CFU occurred after incubation of 2951 gale in either 50 or 25% pooled human serum (PNHS), and CFU in 10% PNHS decreased by about 1 log₁₀ unit. These studies suggest that the Pk epitope of the LOS may be an important factor in the resistance of *M. catarrhalis* to the complement-mediated bactericidal effect of normal human serum.

REFERENCE COUNT: 58
 REFERENCE(S): (1) Aebi, C; Infect Immun 1998, V66, P3113
 CAPLUS
 (2) Alexeyev, M; BioTechniques 1995, V18, P52
 CAPLUS
 (3) Altschul, S; Nucleic Acids Res 1997, V25, P3389 CAPLUS
 (5) Apicella, M; J Infect Dis 1986, V153, P520
 CAPLUS
 (6) Borovkov, A; BioTechniques 1997, V22, P812
 CAPLUS
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2001 ACS
 ACCESSION NUMBER: 2000:603699 CAPLUS
 DOCUMENT NUMBER: 133:280265
 TITLE: Enhancement of clearance of bacteria from murine
 lungs by immunization with detoxified
 lipooligosaccharide from
Moraxella catarrhalis
 conjugated to proteins
 AUTHOR(S): Hu, Wei-Gang; Chen, Jing; Battey, James F.; Gu,
 Xin-Xing
 CORPORATE SOURCE: Laboratory of Immunology, National Institute on

Deafness and Other Communication Disorders,
National Institutes of Health, Rockville, MD,
20850, USA

SOURCE: Infect. Immun. (2000), 68(9), 4980-4985
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Moraxella catarrhalis** strain 25238 detoxified lipooligosaccharide (dLOS)-protein conjugates induced a significant rise of bactericidal anti-LOS antibodies in animals. This study reports the effect of active or passive immunization with the conjugates or their antiserum on pulmonary clearance of **M. catarrhalis** in an aerosol challenge mouse model. Mice were injected s.c. with dLOS-tetanus toxoid (dLOS-TT), dLOS-high-mol.-wt. proteins (dLOS-HMP) from nontypeable *Haemophilus influenzae* (NTHi), or nonconjugated materials in Ribi adjuvant and then challenged with **M. catarrhalis** strain 25238 or O35E or NTHi strain 12. Immunization with dLOS-TT or dLOS-HMP generated a significant rise of serum anti-LOS IgG and 68% and 35 to 41% redns. of bacteria in lungs compared with the control following challenge with homologous strain 25238 and heterologous strain O35E, resp. Serum anti-LOS antibody levels correlated with its bactericidal titers against **M. catarrhalis** and bacterial CFU in lungs. Addnl., immunization with dLOS-HMP generated a 54% redn. of NTHi strain 12 compared with the control. Passive immunization with a rabbit antiserum against dLOS-TT conferred a significant redn. of strain 25238 CFU in lungs in a dose- and time-dependent pattern compared with preimmune serum-treated mice. Kinetic examn. of lung tissue sections demonstrated that antiserum-treated mice initiated and offset inflammatory responses more rapidly than preimmune serum-treated mice. These data indicate that LOS antibodies (whether active or passive) play a major role in the enhancement of pulmonary clearance of different test strains of **M. catarrhalis** in mice. In addn., dLOS-HMP is a potential candidate for a bivalent vaccine against **M. catarrhalis** and NTHi infections.

REFERENCE COUNT: 45

REFERENCE(S): (1) Aderem, A; Annu Rev Immunol 1999, V17, P593
CAPLUS
(3) Barenkamp, S; Infect Immun 1992, V60, P1302
CAPLUS
(5) Barington, T; Infect Immun 1994, V62, P9
CAPLUS
(9) Chen, D; Infect Immun 1996, V64, P1900
CAPLUS
(12) Doern, G; Antimicrob Agents Chemother 1996,

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V40, P2884 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:327769 CAPLUS

TITLE: Strategies for structural determination of
lipo-oligosaccharides using
mass spectrometry.

AUTHOR(S): Gaucher, Sara P.; Leary, Julie A.

CORPORATE SOURCE: Department of Chemistry, University of
California, Berkeley, CA, 94720, USA

SOURCE: Book of Abstracts, 219th ACS National Meeting,
San Francisco, CA, March 26-30, 2000 (2000),
CARB-092. American Chemical Society:
Washington, D. C.
CODEN: 69CLAC

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB **Lipooligosaccharides** embedded in the outer membrane of
many bacteria mediate the initial stages of infection in the host.
Therefore, structural detn. of these antigens is necessary as a
first step in developing glycoconjugate vaccines. Sample
availability is extremely limited in many cases and these
oligosaccharides are quite heterogeneous, making the application of
MS techniques particularly relevant. Here we present the
application of Electrospray Ionization (ESI) and mass anal. using a
Quadrupole Ion Trap (QIT) and Fourier Transform Ion Cyclotron
Resonance (FT-ICR) to investigate **lipooligosaccharides**
from the upper respiratory pathogens *Haemophilus influenzae* and
Moraxella catarrhalis. Multiple stages of mass
spectrometry (MSn) provide information on monosaccharide compn.,
sequence, and linkage using as little as 2 nmol of material. In
addn., structures which display a great deal of microheterogeneity
can also be examd. Because these structures are resolved by m/z
they can be sepd. from one another in the gas phase and examd.
individually by MSn.

L2 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:464181 CAPLUS

DOCUMENT NUMBER: 131:86860

TITLE: **Lipooligosaccharide**-based vaccine for
prevention of *Moraxella* (
Branhamella) *catarrhalis*
infections in mammals

INVENTOR(S): Gu, Xin-Xing; Robbins, John B.

PATENT ASSIGNEE(S): The Government of the United States of America,
Department of Health and Hum, USA

SOURCE: PCT Int. Appl., 60 pp.

Searcher : Shears 308-4994

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CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9936086	A1	19990722	WO 1999-US590	19990112
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9922212	A1	19990802	AU 1999-22212	19990112
BR 9906902	A	20001017	BR 1999-6902	19990112
EP 1047447	A1	20001102	EP 1999-902170	19990112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1998-71483 P 19980113
WO 1999-US590 W 19990112

AB A conjugate vaccine for *Moraxella catarrhalis* comprising isolated lipooligosaccharide from which esterified fatty acids have been removed, to produce a detoxified lipooligosaccharide (dLOS), or from which lipid A has been removed, to produce a detoxified oligosaccharide (OS), which is linked to an immunogenic carrier. The immunogenic carrier is selected from the group consisting of UspA or CD derived from *M. catarrhalis*, tetanus toxoid, HMP derived from *Haemophilus influenza*, diphtheria toxoid, detoxified *P. aeruginosa* toxin A, cholera toxin, pertussis toxin, hepatitis B surface or core antigen, rotavirus VP 7 protein, CRM, CRM197, CRM3201 and respiratory syncytial virus F and G protein. The vaccine is useful for preventing otitis media and respiratory infections caused by *M. catarrhalis* in mammals, including humans.

REFERENCE COUNT: 7

REFERENCE (S): (1) Edebrink, P; CARBOHYDR RES 1995, V266(2), P237 CAPLUS
(2) Gibson, B; WO 9853851 A 1998 CAPLUS
(3) Gu, X; INFECTION AND IMMUNITY 1993, V61(5), P1873 CAPLUS ✓
(4) Gu, X; INFECTION AND IMMUNITY 1996, V64(10), P4047 CAPLUS ✓
(5) Gu, X; INFECTION AND IMMUNITY 1998, V66(5),

Searcher : Shears 308-4994

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P1891 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:800024 CAPLUS
DOCUMENT NUMBER: 130:51336
TITLE: Laft mutants of pathogenic gram-negative
bacteria
INVENTOR(S): Apicella, Michael A.; Gibson, Bradford W.;
Nichols, Wade A.
PATENT ASSIGNEE(S): University of Iowa Research Foundation, USA;
University of California
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9853851	A1	19981203	WO 1998-US10881	19980528
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9877010	A1	19981230	AU 1998-77010	19980528
PRIORITY APPLN. INFO.:			US 1997-47791	19970528
			WO 1998-US10881	19980528

AB A method is provided for identifying, isolating, and producing
lipooligosaccharide (LOS) mutants of gram-neg.
bacterial pathogens. The method comprises mutating the laft gene of
a gram-neg. bacterial pathogen so that there is a lack of a
functional Lipid A fatty acid transferase protein. The resulting
LOS mutants lack one or more secondary acyl chains as compared to
the LOS contained in the wild type gram-neg. bacterial pathogen.
The LOS isolated from the laft mutants displays substantially
reduced toxicity as compared to that of the wild type strain. Also,
the present invention provides methods for using a vaccine
formulation contg. the laft mutants, the endotoxin isolated
therefrom, or the endotoxin isolated therefrom which is then
conjugated to a carrier protein, to immunize an individual against
infections caused by gram-neg. bacterial pathogens by administering

a prophylactically effective amt. of the vaccine formulation.

REFERENCE COUNT: 6
 REFERENCE(S): (1) Clementz; J Biol Chem 1997, V272(16), P10353
 CAPLUS
 (2) Jones; Infect Immun 1997, V65(11), P4778
 CAPLUS
 (3) Lee; J Biol Chem 1995, V270(45), P27151
 CAPLUS
 (4) Somerville; J Clin Invest 1996, V97(2), P359
 CAPLUS
 (5) Sprouse; US 5641492 A 1997 CAPLUS
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2001 ACS

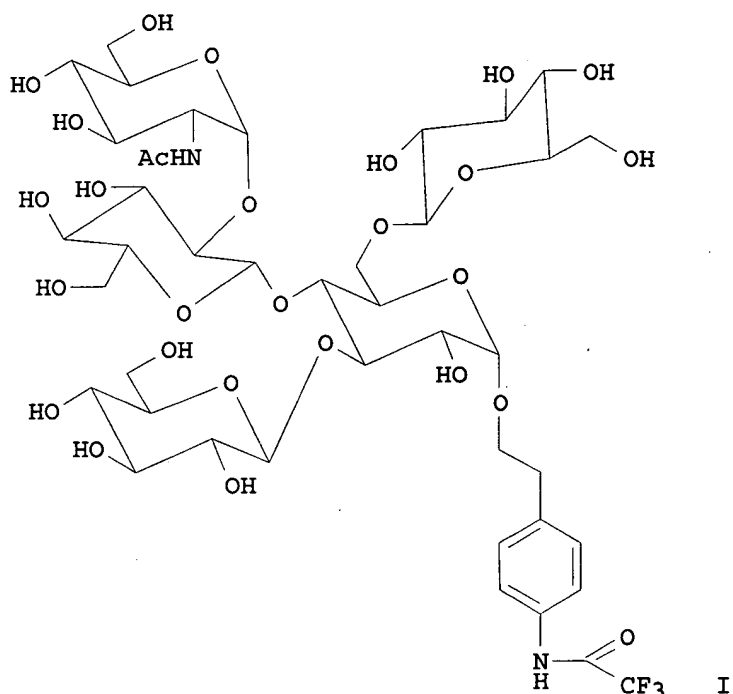
ACCESSION NUMBER: 1998:296912 CAPLUS
 DOCUMENT NUMBER: 129:53186
 TITLE: Synthesis and characterization of
 lipooligosaccharide-based conjugates as
 vaccine candidates for *Moraxella* (
Branhamella) *catarrhalis*
 AUTHOR(S): Gu, Xin-Xing; Chen, Jing; Barenkamp, Stephen J.;
 Robbins, John B.; Tsai, Chao-Ming; Lim, David
 J.; Battey, James
 CORPORATE SOURCE: Laboratory of Immunology, National Institute on
 Deafness and Other Communication Disorders,
 Rockville, MD, 20850, USA
 SOURCE: Infect. Immun. (1998), 66(5), 1891-1897
 CODEN: INFIBR; ISSN: 0019-9567
 PUBLISHER: American Society for Microbiology
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB *Moraxella* (*Branhamella*) *catarrhalis* is
 an important cause of otitis media and sinusitis in children and of
 lower respiratory tract infections in adults.
Lipooligosaccharide (LOS) is a major surface
 antigen of the bacterium and elicits bactericidal antibodies.
 Treatment of the LOS from strain ATCC 25238 with anhyd. hydrazine
 reduced its toxicity 20,000-fold, as assayed in the *Limulus*
 amoebocyte lysate (LAL) test. The detoxified LOS (dLOS) was coupled
 to tetanus toxoid (TT) or high-mol.-wt. proteins (HMP) from
 nontypeable *Haemophilus influenzae* through a linker of adipic acid
 dihydrazide to form dLOS-TT or dLOS-HMP. The molar ratios of dLOS
 to TT and HMP conjugates were 19:1 and 31:1, resp. The antigenicity
 of the two conjugates was similar to that of the LOS, as detd. by
 double immunodiffusion. S.c. or i.m. injection of both conjugates
 elicited a 50- to 100-fold rise in the geometric mean of IgG to the
 homologous LOS in mice after three injections and a 350- to 700-fold
 rise of anti-LOS IgG in rabbits after two injections. The

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immunogenicity of the conjugate was enhanced by formulation with monophosphoryl lipid A plus trehalose dimycolate. In rabbits, conjugate-induced antisera had complement-mediated bactericidal activity against the homologous strain and heterologous strains of *M. catarrhalis*. These results indicate that a detoxified LOS-protein conjugate is a candidate for immunization against *M. catarrhalis* diseases.

L2 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:618939 CAPLUS
DOCUMENT NUMBER: 125:329176
TITLE: Synthesis of Oligosaccharide Structures from the
Lipopolysaccharide of *Moraxella*
catarrhalis
AUTHOR(S): Ekeloef, Kerstin; Oscarson, Stefan
CORPORATE SOURCE: Arrhenius Laboratory, Stockholm University,
Stockholm, S-106 91, Swed.
SOURCE: J. Org Chem. (1996), 61(22), 7711-7718
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB The synthesis of the oligosaccharide I was described. The synthesis of the octasaccharide [p-(trifluoroacetamido)phenyl]ethyl 4-O-[2-O-(2-acetamido-2-deoxy-.alpha.-D-glucopyranosyl)-.beta.-D-glucopyranosyl]-3-O-.beta.-D-glucopyranosyl-6-O-[2-O-[4-O-(4-O-.alpha.-D-galactopyranosyl)-.beta.-D-galactopyranosyl)-.alpha.-D-glucopyranosyl]-.beta.-D-glucopyranosyl]-.alpha.-D-glucopyranoside, representing the outer part of the **lipooligosaccharide** from **Moraxella catarrhalis** serotype A, was described, together with a hepta-, a hexa-, and a pentasaccharide, composing parts thereof with shorter oligosaccharide chains substituted in the 6-position of the central 3,4,6-branched glucose moiety. The versatility of the use of thioglycosides in oligosaccharide synthesis is shown, since throughout the synthesis thioglycosides are used as glycosyl donor precursors, either directly in dimethyl(methylthio)sulfonium triflate (DMTST)-promoted coupling reactions or after conversion to the corresponding glycosyl bromide in silver triflate-promoted couplings. The effects of different protecting groups, anomeric leaving groups, and solvents used in the various coupling reactions are often substantial, which necessitates the use of easily convertible intermediates.

09/610034

ACCESSION NUMBER: 1996:60653 CAPLUS
DOCUMENT NUMBER: 124:169948
TITLE: Separation and characterization of O-deacylated
lipooligosaccharides and glycans derived
from *Moraxella catarrhalis*
using capillary electrophoresis-electrospray
mass spectrometry and tandem mass spectrometry
AUTHOR(S): Kelly, J.; Masoud, H.; Perry, M. B.; Richards,
J. C.; Thibault, P.
CORPORATE SOURCE: Dep. Chem., Dalhousie Univ., Halifax, NS, B3H
4J3, Can.
SOURCE: Anal. Biochem. (1996), 233(1), 15-30
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Electrophoretic methods have been developed for the anal. of complex carbohydrates derived from lipooligosaccharides (LOS) of *Moraxella catarrhalis* using capillary electrophoresis coupled to electrospray mass spectrometry (CE-ESMS). Sepn. of lipooligosaccharides (LOS) arising from mild hydrazinolysis of the intact lipopolysaccharides (LPS) was achieved using aq. ammonium formate, and enabled identification of sites of heterogeneity (phosphates, phosphoethanolamine, and pendant acyl groups) on either the lipid A or the core oligosaccharide. More complex mixts. of carbohydrates obtained from the complete deacylation and dephosphorylation of LOS were amenable to electrophoretic conditions using both anionic and cationic sepn. In particular, electrophoretic conditions were developed which permitted resolu. of closely related oligosaccharides according to the no. of carbohydrate residues appended to the core structure. Structural characterization of carbohydrates and LOS released from the hydrazinolysis and acid hydrolysis treatment of the intact LPS was achieved using tandem mass spectrometry (MS-MS) for samples introduced by direct flow injection. Taken together, the combination of CE-ESI-MS and MS-MS analyses provided valuable information on the heterogeneity of the LOS population in which a significant level of variability was found mostly in the lipid A portion.

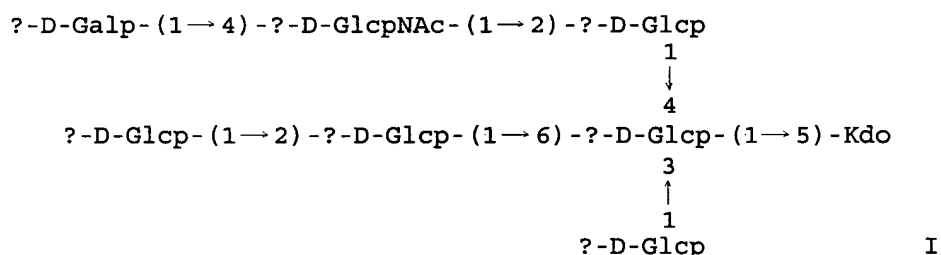
L2 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:320431 CAPLUS
DOCUMENT NUMBER: 122:240278
TITLE: Structural studies of the O-antigen
oligosaccharides from two strains of
Moraxella catarrhalis serotype
C
AUTHOR(S): Edebrink, Per; Jansson, Per-Erik; Mahbubur
Rahman, M.; Widmalm, Goeran; Holme, Tord;

Searcher : Shears 308-4994

09/610034

CORPORATE SOURCE: Rahman, Motiur
Department of Organic Chemistry, Arrhenius
Laboratory, Stockholm University, Stockholm,
S-106-91, Swed.
SOURCE: Carbohydr. Res. (1995), 266(2), 237-61
CODEN: CRBRAT, ISSN: 0008-6215
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB The oligosaccharide parts from *Moraxella* (*Branhamella*) *catarrhalis* serotype C lipooligosaccharides were isolated by mild acid hydrolysis followed by gel permeation chromatog. Four different oligosaccharides, e.g. I, could be identified from strain RS26 and two from strain RS10. The structures of the O-oligosaccharides were established by methylation analyses, mass spectrometry, and NMR spectroscopy. It is concluded that the oligosaccharide O-antigens from RS26 are a mixt. of octa-, deca-, and undeca-saccharides, and most likely a heptasaccharide. Strain RS10 contains the deca- and the undeca-saccharide only. Methylation anal. of the intact lipooligosaccharides showed that two KDO residues were present, one terminal and one 4,5-substituted residue. It also showed that they consisted of a lipid A portion with 6-substituted glucosamine residues.

L2 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:260096 CAPLUS
DOCUMENT NUMBER: 122:38807
TITLE: lipooligosaccharide-depleted antigenic
outer membrane proteins of gram-negative cocci
INVENTOR(S): Zlotnick, Gary W.
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent

Searcher : Shears 308-4994 .

09/610034

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 624376	A1	19941117	EP 1994-106827	19940502
EP 624376	B1	20000315		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 190502	E	20000415	AT 1994-106827	19940502
ES 2145072	T3	20000701	ES 1994-106827	19940502
CA 2123355	AA	19941114	CA 1994-2123355	19940511
JP 08019396	A2	19960123	JP 1994-122032	19940512

PRIORITY APPLN. INFO.: US 1993-61581 A 19930513

AB A method for removing toxic lipooligosaccharide (LOS) from outer membranes of gram-neg. cocci, such as *Neisseria meningitidis*, is presented. Total membranes of the coccus are extd. with PEG to produce outer membranes depleted of inner membranes; the outer membranes are then extd. with a zwitterionic betaine detergent to remove LOS. The LOS-depleted outer membranes are able to elicit bactericidal antibodies against homologous strains of bacteria, and are useful in vaccines.

L2 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1992:527885 CAPLUS

DOCUMENT NUMBER: 117:127885

TITLE: Further antigenic similarities of *Neisseria gonorrhoeae* lipooligosaccharides and human glycosphingolipids

AUTHOR(S): Mandrell, Robert E.

CORPORATE SOURCE: Cent. Immunochem., Veterans Adm. Med. Cent., San Francisco, CA, 94121, USA

SOURCE: Infect. Immun. (1992), 60(7), 3017-20

CODEN: INFIBR; ISSN: 0019-9567

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Anticarbhydrate monoclonal antibodies were tested for their ability to bind to various strains of *Neisseria*. A monoclonal antibody that binds to the ganglio-series glycosphingolipid, ganglio-N-triaosylceramide, also bound to strains of *N. gonorrhoeae* but not to other species of *Neisseria*. An antibody specific for the globo-series glycosphingolipid, globotriaosylceramide, also bound to strains of *N. gonorrhoeae*, *N. meningitidis*, *N. lactamica*, and *Branhamella catarrhalis* but not to any other strains of nonpathogenic *Neisseria*.

L2 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2001 ACS

Searcher : Shears 308-4994

ACCESSION NUMBER: 1998234010 MEDLINE
DOCUMENT NUMBER: 98234010 PubMed ID: 9573066
TITLE: Synthesis and characterization of lipooligosaccharide-based
conjugates as vaccine candidates for *Moraxella*
(*Branhamella*) *catarrhalis*.
AUTHOR: Gu X X; Chen J; Barenkamp S J; Robbins J B; Tsai C M; Lim D
J; Battey J
CORPORATE SOURCE: Laboratory of Immunology, National Institute on Deafness
and Other Communication Disorders, Rockville, Maryland
20850, USA.. xgu@pop.nidcd.nih.gov
SOURCE: INFECTION AND IMMUNITY, (1998 May) 66 (5) 1891-7.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980520
Last Updated on STN: 19980520
Entered Medline: 19980514

AB *Moraxella* (*Branhamella*) *catarrhalis* is an important cause of otitis media and sinusitis in children and of lower respiratory tract infections in adults. Lipooligosaccharide (LOS) is a major surface antigen of the bacterium and elicits bactericidal antibodies. Treatment of the LOS from strain ATCC 25238 with anhydrous hydrazine reduced its toxicity 20,000-fold, as assayed in the *Limulus* amoebocyte lysate (LAL) test. The detoxified LOS (dLOS) was coupled to tetanus toxoid (TT) or high-molecular-weight proteins (HMP) from nontypeable *Haemophilus influenzae* through a linker of adipic acid dihydrazide to form dLOS-TT or dLOS-HMP. The molar ratios of dLOS to TT and HMP conjugates were 19:1 and 31:1, respectively. The antigenicity of the two conjugates was similar to that of the LOS, as determined by double immunodiffusion. Subcutaneous or intramuscular injection of both conjugates elicited a 50- to 100-fold rise in the geometric mean of immunoglobulin G (IgG) to the homologous LOS in mice after three injections and a 350- to 700-fold rise of anti-LOS IgG in rabbits after two injections. The immunogenicity of the conjugate was enhanced by formulation with monophosphoryl lipid A plus trehalose dimycolate. In rabbits, conjugate-induced antisera had complement-mediated bactericidal activity against the homologous strain and heterologous strains of *M. catarrhalis*. These results indicate that a **detoxified** LOS-protein conjugate is a candidate for immunization against *M. catarrhalis* diseases.

09/610034

ACCESSION NUMBER: 1991:40563 CAPLUS
DOCUMENT NUMBER: 114:40563
TITLE: **Lipooligosaccharide** epitopes shared
among gram-negative non-enteric mucosal
pathogens
AUTHOR(S): Campagnari, Anthony A.; Spinola, Stanley M.;
Lesse, Alan J.; Kwaik, Yousef Abu; Mandrell,
Robert E.; Apicella, Michael A.
CORPORATE SOURCE: Sch. Med., State Univ. New York, Buffalo, NY,
USA
SOURCE: Microb. Pathog. (1990), 8(5), 353-62
CODEN: MIPAEV; ISSN: 0882-4010
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The non-enteric Gram-neg. human pathogens, **Branhamella**
catarrhalis, *Haemophilus ducreyi*, *H. influenzae*, *Neisseria*
gonorrhoeae, and *N. meningitidis*, do not have repeating O-antigens
as part of their principal surface glycolipid, the
lipooligosaccharide (LOS). Because they have
similar LOS structures, the authors studied the conservation of LOS
oligosaccharide epitopes among these organisms. Twenty-one
monoclonal antibodies (mAbs) generated by immunizing mice with *H.*
influenzae, *N. gonorrhoeae*, and *N. meningitidis* were studied for
cross reactivity. Five mAbs generated against non-typable *H.*
influenzae were the only strain-specific antibodies. Ten mAbs
reacted to LOS epitope(s) common to a genus or species, and 6 mAbs
bound to epitope(s) on the LOS of strains from different genera.
Some cross reactive mAbs bound to LOS bands of similar mol. wts.,
while others bound to bands of varying mol. wts. Mab 3F11, whose
epitope mimics a human blood-group antigen, bound to a 4.8 kDa LOS
band in *N. gonorrhoeae* and *H. ducreyi*, 2 pathogens that infect
genital epithelium. Mab 3D9, whose epitope consists of
2-keto-3-deoxyoctulosonic acid (KDO), reacted with different LOS
bands in *N. gonorrhoeae*, *H. influenzae*, and some R mutants of *S.*
minnesota. A 14 kb restriction fragment contg.
lipooligosaccharide synthesis genes responsible for the
assembly of the 3D9 epitope in *H. influenzae* hybridized to all *H.*
influenzae strains tested but did not hybridize to gonococcal and *S.*
minnesota strains that expressed this epitope. Thus, conserved LOS
epitope(s) exist among different species and genera of non-enteric
human pathogens and different genetic mechanisms may have evolved in
these pathogens to assemble some of these conserved epitopes.

(FILE 'CAPLUS' ENTERED AT 11:47:41 ON 25 JUL 2001)

L3 14 SEA ABB=ON PLU=ON CATARRHAL? AND (LOS(S) (LIPOOLIGO? OR
LIPO OLIGO?) OR LIPOOLIGOSACCHARID? OR LIPO(W) (OLIGOSACCH
ARID? OR OLIGO SACCHARID?) OR LIPOOLIGO SACCHARID?)
L4 0 SEA ABB=ON PLU=ON L3 NOT L2

Searcher : Shears 308-4994

09/610034

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
JICST-EPLUS, JAPIO' ENTERED AT 11:52:27 ON 25 JUL 2001)

L5 76 S L3

L6 35 DUP REM L5 (41 DUPLICATES REMOVED)

L6 ANSWER 1 OF 35 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001285352 MEDLINE
DOCUMENT NUMBER: 21116943 PubMed ID: 11179299
TITLE: Functional characteristics of a protective monoclonal
antibody against serotype A and C
lipooligosaccharides from *Moraxella*
catarrhalis.
AUTHOR: Hu W G; Chen J; McMichael J C; Gu X X
CORPORATE SOURCE: Laboratory of Immunology, National Institute on
Deafness and Other Communication Disorders,
Rockville, Maryland 20850, USA.
SOURCE: INFECTION AND IMMUNITY, (2001 Mar) 69 (3) 1358-63.
Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20010529
Entered Medline: 20010524

AB A monoclonal antibody (MAB), designated MAb 8E7 (immunoglobulin G3),
specific for *Moraxella catarrhalis*
lipooligosaccharide (LOS) was evaluated for its
functional activity in vitro and in a mouse model of colonization.
Enzyme-linked immunosorbent assay (ELISA) demonstrated that the MAB
8E7 could be prepared to a high titer against LOS of the
homologous strain O35E, and that it had bactericidal activity. MAB
8E7 reacted with *M. catarrhalis* serotype A and C LOSs but
not serotype B LOS, as measured by ELISA and Western
blotting. On the basis of published structures of LOSs, this
suggests that the epitope recognized by MAB 8E7 is directed to a
common sequence of either alpha-GlcNAc-(1-->2)-beta-Glc-(1--> at the
branch substituting position 4 of the trisubstituted Glc residue or
a terminal tetrasaccharide alpha-Gal-(1-->4)-beta-Gal-(1-->4)-alpha-
Glc-(1-->2)-beta-Glc-(1--> at the branch substituting position 6 of
the trisubstituted Glc residue. In a whole-cell ELISA, MAB 8E7
reacted with 70% of the 30 wild-type strains and clinical isolates
tested. Immuno-electron microscopy demonstrated that MAB 8E7 reacted
with a cell surface-exposed epitope of LOS on strain O35E.
MAB 8E7 inhibited the adherence of strain O35E to Chang conjunctival
epithelial cells by 90%. Passive immunization with MAB 8E7 could

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significantly enhance the clearance of strain O35E from mouse lungs in an aerosol challenge mouse model. This enhanced bacterial clearance was inhibited when MAb 8E7 was absorbed by M. *catarrhalis* serotype A LOS, indicating that the M. *catarrhalis* LOS-directed antibody may play a major role in the enhancement of M. *catarrhalis* clearance from lungs. These data suggest that MAb 8E7, which recognizes surface-exposed LOS of M. *catarrhalis*, is a protective antibody against M. *catarrhalis*.

L6 ANSWER 2 OF 35 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001231775 EMBASE
TITLE: Molecular mimicry of host structures by
lipooligosaccharides of Neisseria
meningitidis: Characterization of sialylated and
nonsialylated lacto-N-neotetraose
(Gal.beta.1-4GlcNAc.beta.1-3Gal.beta.1-4Glc)
structures in lipooligosaccharides using
monoclonal antibodies and specific lectins.
AUTHOR: Tsai C.-M.
CORPORATE SOURCE: C.-M. Tsai, Division of Bacterial Products, Ctr. for
Biologics Evaluation/Res., FDA, Bethesda, MD 20892,
United States
SOURCE: Advances in Experimental Medicine and Biology, (2001)
491/- (525-542).
Refs: 79
ISSN: 0065-2598 CODEN: AEMBAP
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Neisseria meningitidis lipooligosaccharides (LOSs) are classified into 12 immunotypes. Most LOSs are heterogeneous in having a few components by SDS-PAGE analysis that differ antigenically and chemically. We have utilized a monoclonal antibody that recognizes lacto-N-neotetraose (LNnT) and the lectin, Maackia amurensis leucoagglutinin (MAL), which is specific for NeuNAc.alpha.2-3Gal.beta.1-4GlcNAc trisacchride sequence to characterize the 12 N. meningitidis LOSs. Using the combination of ELISA, SDS-PAGE, Western blotting, and other chemical analyses, we have shown that the LNnT (Gal.beta.1-4GlcNAc.beta.1-3Gal.beta.1-4Glc) sequence was present in the 4.0-kDa LOS components of seven immunotype LOSs seen on SDS-PAGE. Six of the seven LNnT-containing LOSs also bound the MAL lectin indicating that N-acetylneuraminic acid (NeuNAc) was .alpha.2,3-linked to the LNnT

sequence in the LOSs. Sialylation of the terminal Gal of LNnT-containing 4.0-kDa component caused only a slight increase in its apparent MW to 4100 on SDS-PAGE. The one LOS with the LNnT-containing component, but not MAL-binding, was from a Group A *N. meningitidis*, which does not synthesize CMP-NeuNAc, the substrate needed for LOS sialylation. Thus, it is concluded (1) a common LNnT sequence is present in seven immunotype LOSs in addition to their immunotype epitopes, and (2) NeuNAc is .alpha.2->3 linked to the terminal Gal of LNnT if a organism synthesizes CMP-NeuNAc such as Groups B and C organisms. The above conclusions are consistent with the published structures of *N. meningitidis* LOSs. The results also demonstrate that specific carbohydrate-binding lectins and monoclonal antibodies can be used as simple yet effective tools to characterize specific carbohydrate sequences in a bacterial LOS or LPS such as *N. meningitidis* LOS

. It is intriguing that *N. meningitidis* LOSs mimic certain glycosphingolipids, such as paragloboside (LNnT-ceramide) and sialylparagloboside, and some glycoproteins of the host in having LNnT and N-acetylactosamine sequences respectively with or without .alpha.2->3 linked NeuNAc. Epidemiological studies of *N. meningitidis* suggest that the molecular mimicry of host structures by its LOS plays a role in the pathogenesis of *N. meningitidis* by helping the organism to evade host immune defenses in man. The molecular mimicry of host structures by LOS or LPS is also found in other human pathogens such as *N. gonorrhoeae*, *Haemophilus ducreyi*, *H. influenzae*, *Moraxella catarrhalis*, *Campylobacter jejuni*, and *Helicobacter pylori*.

L6	ANSWER 3 OF 35	MEDLINE	DUPLICATE 2
ACCESSION NUMBER:	2000428085	MEDLINE	
DOCUMENT NUMBER:	20407342	PubMed ID: 10948153	
TITLE:	Lipooligosaccharide P(k) (Galalpha1-4Galbeta1-4Glc) epitope of moraxella catarrhalis is a factor in resistance to bactericidal activity mediated by normal human serum.		
AUTHOR:	Zaleski A; Scheffler N K; Densen P; Lee F K; Campagnari A A; Gibson B W; Apicella M A		
CORPORATE SOURCE:	Department of Microbiology, The University of Iowa, Iowa City, Iowa 52242, USA.		
CONTRACT NUMBER:	AI44642 (NIAID) AI45728 (NIAID) AI46469 (NIAID) +		
SOURCE:	INFECTION AND IMMUNITY, (2000 Sep) 68 (9) 5261-8. Journal code: GO7; 0246127. ISSN: 0019-9567.		
PUB. COUNTRY:	United States		
LANGUAGE:	Journal; Article; (JOURNAL ARTICLE)		
	English		

09/610034

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000908

AB *Moraxella catarrhalis* is a respiratory pathogen responsible for acute bacterial otitis media in children and exacerbation of chronic bronchitis in adults. *M. catarrhalis* strains are frequently resistant to the bactericidal activity of normal human serum. In order to determine if the lipooligosaccharide (LOS) of *M. catarrhalis* has a role in serum resistance, the UDP-glucose-4-epimerase (gale) gene was identified, cloned, and sequenced and a deletion/insertion mutation was introduced into *M. catarrhalis* strain 2951. Gale enzymatic activity, measured in whole-cell lysates, was ablated in *M. catarrhalis* 2951 gale. Mass spectrometric analysis of LOS isolated with hot phenol-water confirmed that strain 2951 produced a type A LOS. These studies showed that the LOS from 2951 gale had lost two hexose residues due to the gale mutation and that the resultant LOS structure lacked the (Gal α 1-4Gal β 1-4Glc) P(k) epitope found on *M. catarrhalis* 2951. Wild-type *M. catarrhalis* 2951 is resistant to complement-mediated serum bactericidal activity. In contrast, a greater than 2-log(10)-unit reduction in CFU occurred after incubation of 2951 gale in either 50 or 25% pooled human serum (PNHS), and CFU in 10% PNHS decreased by about 1 log(10) unit. These studies suggest that the P(k) epitope of the LOS may be an important factor in the resistance of *M. catarrhalis* to the complement-mediated bactericidal effect of normal human serum.

L6 ANSWER 4 OF 35 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2000428046 MEDLINE
DOCUMENT NUMBER: 20407303 PubMed ID: 10948114
TITLE: Enhancement of clearance of bacteria from murine lungs by immunization with detoxified lipooligosaccharide from *Moraxella catarrhalis* conjugated to proteins.
AUTHOR: Hu W G; Chen J; Battey J F; Gu X X
CORPORATE SOURCE: Laboratory of Immunology, National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Rockville, Maryland 20850, USA.
SOURCE: INFECTION AND IMMUNITY, (2000 Sep) 68 (9) 4980-5.
Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

Searcher : Shears 308-4994

09/610034

ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000908

AB *Moraxella catarrhalis* strain 25238 detoxified lipooligosaccharide (dLOS)-protein conjugates induced a significant rise of bactericidal anti-LOS antibodies in animals. This study reports the effect of active or passive immunization with the conjugates or their antiserum on pulmonary clearance of *M. catarrhalis* in an aerosol challenge mouse model. Mice were injected subcutaneously with dLOS-tetanus toxoid (dLOS-TT), dLOS-high-molecular-weight proteins (dLOS-HMP) from nontypeable *Haemophilus influenzae* (NTHi), or nonconjugated materials in Ribi adjuvant and then challenged with *M. catarrhalis* strain 25238 or O35E or NTHi strain 12. Immunization with dLOS-TT or dLOS-HMP generated a significant rise of serum anti-LOS immunoglobulin G and 68% and 35 to 41% reductions of bacteria in lungs compared with the control ($P < 0.01$) following challenge with homologous strain 25238 and heterologous strain O35E, respectively. Serum anti-LOS antibody levels correlated with its bactericidal titers against *M. catarrhalis* and bacterial CFU in lungs. Additionally, immunization with dLOS-HMP generated a 54% reduction of NTHi strain 12 compared with the control ($P < 0.01$). Passive immunization with a rabbit antiserum against dLOS-TT conferred a significant reduction of strain 25238 CFU in lungs in a dose- and time-dependent pattern compared with preimmune serum-treated mice. Kinetic examination of lung tissue sections demonstrated that antiserum-treated mice initiated and offset inflammatory responses more rapidly than preimmune serum-treated mice. These data indicate that LOS antibodies (whether active or passive) play a major role in the enhancement of pulmonary clearance of different test strains of *M. catarrhalis* in mice. In addition, dLOS-HMP is a potential candidate for a bivalent vaccine against *M. catarrhalis* and NTHi infections.

L6 ANSWER 5 OF 35 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2000:155974 SCISEARCH
THE GENUINE ARTICLE: 285UW
TITLE: Serum resistance in *Haemophilus ducreyi* requires outer membrane protein DsrA
AUTHOR: Elkins C (Reprint); Morrow K J; Olsen B
CORPORATE SOURCE: UNIV N CAROLINA, SCH MED, DEPT MED, ROOM 521 BURNETT WOMACK, CAMPUS BOX 7030, CHAPEL HILL, NC 27599 (Reprint); UNIV N CAROLINA, SCH MED, DEPT MICROBIOL & IMMUNOL, CHAPEL HILL, NC 27599; TEXAS TECH UNIV, HLTH SCI CTR, DEPT BIOCHEM & CELL BIOL, LUBBOCK, TX 79430

Searcher : Shears 308-4994

09/610034

COUNTRY OF AUTHOR: USA
SOURCE: INFECTION AND IMMUNITY, (MAR 2000) Vol. 68, No. 3,
pp. 1608-1619.
Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS
AVENUE, NW, WASHINGTON, DC 20005-4171.
ISSN: 0019-9567.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 56

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Haemophilus ducreyi is resistant to killing by normal serum antibody and complement. We discovered an H. ducreyi outer membrane protein required for expression of serum resistance and termed it DsrA (for 'ducreyi serum resistance A'). The dsrA locus was cloned, sequenced, and mutagenized. An isogenic mutant (FX517) of parent strain 35000 was constructed and characterized, and it was found to no longer express dsrA. FX517 was at least 10-fold more serum susceptible than 35000. DsrA was expressed by all strains of H. ducreyi tested, except three naturally occurring, avirulent, serum-sensitive strains. FX517 and the three naturally occurring dsrA-nonexpressing strains were complemented in trans with a plasmid expressing dsrA. All four strains were converted to a serum-resistant phenotype, including two that contained truncated lipooligosaccharide (LOS). Therefore, serum resistance in H. ducreyi does not require expression of full-length LOS but does require expression of dsrA. The dsrA locus from eight additional H. ducreyi strains was sequenced, and the deduced amino acid sequences were more than 85% identical. The major difference between the DsrA proteins was due to the presence of one, two, or three copies of the heptameric amino acid repeat NTHNINK. These repeats account for the variability in apparent molecular mass of the monomeric form of DsrA (28 to 35 kDa) observed in sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Since DsrA is present in virulent strains, is highly conserved, and is required for serum resistance, we speculate that it may be a virulence factor and a potential vaccine candidate.

L6 ANSWER 6 OF 35 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000325744 MEDLINE
DOCUMENT NUMBER: 20325744 PubMed ID: 10865201
TITLE: Progress toward the development of a vaccine to
prevent Moraxella (Branhamella) catarrhalis
infections.
AUTHOR: McMichael J C
CORPORATE SOURCE: Wyeth-Lederle Vaccines, 211 Bailey Road, West
Henrietta, NY 14586-9728, USA.
SOURCE: Microbes Infect, (2000 Apr) 2 (5) 561-8. Ref: 61

Searcher : Shears 308-4994

09/610034

JOURNAL code: DJ1; 100883508. ISSN: 1286-4579.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000811
Last Updated on STN: 20000811
Entered Medline: 20000802

AB *Moraxella catarrhalis* is a major cause of otitis media and respiratory disease. Vaccine development is at the antigen identification stage. This review examines the more promising antigens, including the 200K protein, the hemagglutinins, the lactoferrin-binding proteins, the UspA proteins, the CopB protein, the transferrin-binding proteins, the CD protein, the E protein and lipooligosaccharide conjugates. Clinical testing of some of these antigens should begin soon.

L6 ANSWER 7 OF 35 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:386220 BIOSIS
DOCUMENT NUMBER: PREV200000386220
TITLE: Evaluation of detoxified lipooligosaccharide from *Moraxella catarrhalis* conjugated to proteins as a vaccine in an aerosol challenge mouse model.
AUTHOR(S): Hu, W. G. (1); Chen, J. (1); Gu, X. X. (1)
CORPORATE SOURCE: (1) National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Rockville, MD USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2000) Vol. 100, pp. 300. print.
Meeting Info.: 100th General Meeting of the American Society for Microbiology Los Angeles, California, USA May 21-25, 2000 American Society for Microbiology . ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L6 ANSWER 8 OF 35 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2001381129 MEDLINE
DOCUMENT NUMBER: 21108937 PubMed ID: 11163472
TITLE: Vaccines for *Moraxella catarrhalis*.
AUTHOR: McMichael J C
CORPORATE SOURCE: Wyeth-Lederle Vaccines, 211 Bailey Road, West

Searcher : Shears 308-4994

SOURCE: Henrietta, NY 14586-9728, USA.. mcmichj@war.wyeth.com
 VACCINE, (2000 Dec 8) 19 Suppl 1 S101-7. Ref: 53
 Journal code: X60; 8406899. ISSN: 0264-410X.

PUB. COUNTRY: England: United Kingdom
 Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200107

ENTRY DATE: Entered STN: 20010709
 Last Updated on STN: 20010709
 Entered Medline: 20010705

AB Vaccine development for *Moraxella catarrhalis* is in the antigen identification stage. *M. catarrhalis* does not appear to synthesize secreted antigens such as exotoxins, nor does it appear to possess a carbohydrate capsule. Modified forms of these antigens are usually good vaccine components. There is some interest in whole bacterial cells and membrane fractions, but the search has largely focused on purified outer surface antigens. All of the present antigens have been selected based on the response seen in animals, although the antibody response seen in people exposed to the bacterium provides some guidance. The antibody response provides information related to the cross-strain preservation of epitopes and whether they are surface exposed. Antigens that elicit antibodies that have complement dependent bactericidal capacity, opsonophagocytic activity or interfere with one of the antigen's known functions such as adhesion or nutrient acquisition are particularly valued. In addition to examining the antibody response, some antigens have been evaluated in a murine pulmonary clearance model. Using these assays and model, several vaccine candidates have been identified. The antigens may be roughly classified by the function they serve the bacterium. One set appears to promote adhesion to host tissues and includes the hemagglutinins, ubiquitous surface protein A1 (UspA1), and possibly the CD protein. A second set is involved in nutrient acquisition. This set includes the lactoferrin binding protein A (LbpA) and lactoferrin binding protein B (LbpB), the transferrin binding protein A (TbpA) and transferrin binding protein B (TbpB), the CD and E porins, and the *Catarrhalis* outer membrane protein B (CopB). A third set is comprised of antigens involved in virulence and it includes lipooligosaccharide (LOS) and the ubiquitous surface protein A2 (UspA2). Antigens of unknown function, such as the 200K protein, may also be vaccine candidates. The antigens that are most suitable will be determined in clinical studies that are only beginning now.

09/610034

ACCESSION NUMBER: 1999-444322 [37] WPIDS
DOC. NO. CPI: C1999-130893
TITLE: Detoxified lipooligosaccharide-based
vaccine for prevention of Moraxella
catarrhalis infections in mammals.
DERWENT CLASS: B04-D16
INVENTOR(S): GU, X; ROBBINS, J B
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9936086	A1	19990722	(199937)*	EN	60
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9922212	A	19990802	(199954)		
BR 9906902	A	20001017	(200056)		
EP 1047447	A1	20001102	(200056)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
CN 1288384	A	20010321	(200137)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9936086	A1	WO 1999-US590	19990112
AU 9922212	A	AU 1999-22212	19990112
BR 9906902	A	BR 1999-6902	19990112
		WO 1999-US590	19990112
EP 1047447	A1	EP 1999-902170	19990112
		WO 1999-US590	19990112
CN 1288384	A	CN 1999-802142	19990112

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9922212	A Based on	WO 9936086
BR 9906902	A Based on	WO 9936086
EP 1047447	A1 Based on	WO 9936086

PRIORITY APPLN. INFO: US 1998-71483 19980113
AN 1999-444322 [37] WPIDS

Searcher : Shears 308-4994

AB WO 9936086 A UPAB: 19990914

NOVELTY - A **lipooligosaccharide (LOS)** isolated from *Moraxella catarrhalis* and detoxified by removal of ester-linked fatty acids to produce detoxified **LOS (dLOS)** or treated to remove lipid A to produce oligosaccharide (OS) is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for a conjugate vaccine for *M. catarrhalis* comprising dLOS or OS, and a covalently linked immunogenic carrier as above; methods of detoxifying LOS isolated from *M. catarrhalis*, by removal of ester-linked fatty acids; methods of making a conjugate vaccine as above.

ACTIVITY - Immunoprotective; Auditory; Antibacterial.

MECHANISM OF ACTION - Vaccine.

USE - The methods are useful for isolation of detoxified **lipooligosaccharide** or oligosaccharide from *M. catarrhalis*. The detoxified **lipooligosaccharide** or oligosaccharide are useful in conjugate vaccines. The vaccine is useful for protection against *M. catarrhalis* which causes otitis media and respiratory infections.

ADVANTAGE - The invention provides a detoxified **lipooligosaccharide** from *M. catarrhalis*, the major virulence factor for pathogenesis of bacterial infections. When tested by the standard Limulus amebocyte lysate assay, the isolated **LOS** showed 2×10^4 EU/ μ g, whereas the dLOS showed 1 EU/ μ g, representing a 20000-fold reduction of toxicity.
Dwg.0/3

L6 ANSWER 10 OF 35 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1999-070180 [06] WPIDS
 DOC. NO. CPI: C1999-020714
 TITLE: New laft mutants of gram-negative pathogenic bacteria - produce LOS having reduced toxicity, but retaining antigenicity, useful for immunisation against gram negative bacteria.
 DERWENT CLASS: B04 D16
 INVENTOR(S): APICELLA, M A; GIBSON, B W; NICHOLS, W A
 PATENT ASSIGNEE(S): (APIC-I) APICELLA M A; (GIBS-I) GIBSON B W; (NICH-I) NICHOLS W A; (REGC) UNIV CALIFORNIA; (IOWA) UNIV IOWA RES FOUND
 COUNTRY COUNT: 82
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9853851	A1	19981203	(199906)*	EN	17
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC					
MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI					

09/610034

GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT
LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
TJ TM TR TT UA UG US UZ VN YU ZW
AU 9877010 A 19981230 (199918)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9853851	A1	WO 1998-US10881	19980528
AU 9877010	A	AU 1998-77010	19980528

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9877010	A Based on	WO 9853851

PRIORITY APPLN. INFO: US 1997-47791 19970528

AN 1999-070180 [06] WPIDS

AB WO 9853851 A UPAB: 19990316

A bacterium (I), particularly a Gram negative bacterium, that has its Lipid A fatty transferase (LAft) gene mutated to remove transferase activity (designated a laft mutant), is new. Also claimed are: (1) an endotoxin isolated from a laft mutant bacterium (2) a method of preparing mutant endotoxin, by isolating it from (I), where the mutated endotoxin has substantially reduced toxicity relative to that from the corresponding wild-type bacterium (3) a vaccine comprising: (a) a laft mutant bacterium, particularly where the bacterium is live and inactivated; (b) a physiological carrier suitable for mucosal administration.

USE - (I) is used to immunise an individual, particularly a human against a live gram negative bacterial pathogen (claimed). Gram negative pathogens including *Neisseria meningitides*, *N. gonorrhoeae*, *Haemophilus* species including *H. influenzae* and *H. ducreyi*, and *Moraxella catarrhalis* are particular targets for the vaccine, especially *H. influenzae*. Laft mutants can be engineered to express heterologous antigens of other microbial pathogens at the surface of the mutated bacteria for use as a multivalent vaccine. Isolated endotoxin from laft mutants, either alone, or conjugated to a carrier protein, may be used to generate lipooligosaccharides (LOS)-specific antibodies for passive immunisation and for diagnostic assays to detect gram-negative pathogens in clinical specimens (disclosed).

Dwg.0/1

L6 ANSWER 11 OF 35

MEDLINE

DUPLICATE 6

Searcher : Shears 308-4994

09/610034

ACCESSION NUMBER: 1998234010 MEDLINE
DOCUMENT NUMBER: 98234010 PubMed ID: 9573066
TITLE: Synthesis and characterization of
lipooligosaccharide-based conjugates as
vaccine candidates for Moraxella (Branhamella)
catarrhalis.
AUTHOR: Gu X X; Chen J; Barenkamp S J; Robbins J B; Tsai C M;
Lim D J; Battey J
CORPORATE SOURCE: Laboratory of Immunology, National Institute on
Deafness and Other Communication Disorders,
Rockville, Maryland 20850, USA..
xgu@pop.nidcd.nih.gov
SOURCE: INFECTION AND IMMUNITY, (1998 May) 66 (5) 1891-7.
Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980520
Last Updated on STN: 19980520
Entered Medline: 19980514

AB Moraxella (Branhamella) catarrhalis is an important cause of otitis media and sinusitis in children and of lower respiratory tract infections in adults. Lipooligosaccharide (LOS) is a major surface antigen of the bacterium and elicits bactericidal antibodies. Treatment of the LOS from strain ATCC 25238 with anhydrous hydrazine reduced its toxicity 20,000-fold, as assayed in the Limulus amoebocyte lysate (LAL) test. The detoxified LOS (dLOS) was coupled to tetanus toxoid (TT) or high-molecular-weight proteins (HMP) from nontypeable Haemophilus influenzae through a linker of adipic acid dihydrazide to form dLOS-TT or dLOS-HMP. The molar ratios of dLOS to TT and HMP conjugates were 19:1 and 31:1, respectively. The antigenicity of the two conjugates was similar to that of the LOS, as determined by double immunodiffusion. Subcutaneous or intramuscular injection of both conjugates elicited a 50- to 100-fold rise in the geometric mean of immunoglobulin G (IgG) to the homologous LOS in mice after three injections and a 350- to 700-fold rise of anti-LOS IgG in rabbits after two injections. The immunogenicity of the conjugate was enhanced by formulation with monophosphoryl lipid A plus trehalose dimycolate. In rabbits, conjugate-induced antisera had complement-mediated bactericidal activity against the homologous strain and heterologous strains of M. catarrhalis. These results indicate that a detoxified LOS-protein conjugate is a candidate for immunization against M. catarrhalis diseases.

09/610034

L6 ANSWER 12 OF 35 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1998:428529 SCISEARCH
THE GENUINE ARTICLE: ZQ663
TITLE: Monoclonal antibodies to the epitope
alpha-Gal-(1-4)-beta-Gal-(1- of Moraxella
catarrhalis LPS react with a similar epitope
in type IV pili of Neisseria meningitidis
AUTHOR: Rahman M (Reprint); Jonsson A B; Holme T
CORPORATE SOURCE: ICDDR, DIV SCI LAB, GPO BOX 128, DHAKA, BANGLADESH
(Reprint); KAROLINSKA INST, MICROBIOL & TUMORBIOL
CTR, S-17177 STOCKHOLM, SWEDEN
COUNTRY OF AUTHOR: BANGLADESH; SWEDEN
SOURCE: MICROBIAL PATHOGENESIS, (MAY 1998) Vol. 24, No. 5,
pp. 299-308.
Publisher: ACADEMIC PRESS LTD, 24-28 OVAL RD, LONDON
NW1 7DX, ENGLAND.
ISSN: 0882-4010.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 28

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Murine monoclonal antibodies (MAbs) against the A, B and C LPS serotypes of M. **catarrhalis** were generated and their binding specificity was examined in an enzyme-linked immunosorbent assay (ELISA). Two broadly cross-reactive monoclonal antibodies (MCA1 and MCC2) against the outer core region of LPS were further characterized. A panel of synthetic glycoproteins and glycolipids was used to determine the binding specificity of the MAbs. MCA1 and MCC2 bound specifically to alpha-Gal-(1-4)-beta-Gal of galabiose and globotriose glycoconjugates. The reactivity of the MAbs with galabiose was higher than that with globotriose. The MAbs could recognize the alpha-Gal-(1-4)-beta-Gal epitope only when it was in a terminal position. MCA1 was further shown to react with a similar epitope in the glycosylated type IV pili of N. meningitidis, which has been shown to contain a 1-4 linked digalactose at the terminal part of the saccharide present in the pili. MCA1 could efficiently recognize this epitope indicating that it was exposed on the surface of the pili. (C) 1998 Academic Press Limited.

L6 ANSWER 13 OF 35 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:416635 BIOSIS
DOCUMENT NUMBER: PREV199800416635
TITLE: Characterization of lipooligosaccharide
-based conjugates as vaccine candidates for moraxella
(Branhamella) **catarrhalis**.
AUTHOR(S): Chen, J.; Gu, X-X.
CORPORATE SOURCE: NIDCD/NIH, Rockville, MD USA

Searcher : Shears 308-4994

09/610034

SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (1998) Vol. 98, pp. 236. Meeting Info.: 98th General Meeting of the American Society for Microbiology Atlanta, Georgia, USA May 17-21, 1998 American Society for Microbiology . ISSN: 1060-2011.

DOCUMENT TYPE: Conference

LANGUAGE: English

L6 ANSWER 14 OF 35 MEDLINE DUPLICATE 7

ACCESSION NUMBER: 1999094568 MEDLINE

DOCUMENT NUMBER: 99094568 PubMed ID: 9879959

TITLE: Outer-membrane antigen expression by *Moraxella* (*Branhamella*) **catarrhalis** influences pulmonary clearance.

AUTHOR: Kyd J M; Cripps A W; Murphy T F

CORPORATE SOURCE: Faculty of Applied Science, University of Canberra, Belconnen, Australian Capital Territory.

CONTRACT NUMBER: AI28304 (NIAID)
TW02158 (FIC)

SOURCE: JOURNAL OF MEDICAL MICROBIOLOGY, (1998 Feb) 47 (2) 159-68.
Journal code: J2N; 0224131. ISSN: 0022-2615.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199901

ENTRY DATE: Entered STN: 19990128
Last Updated on STN: 19990128
Entered Medline: 19990111

AB *Moraxella* (*Branhamella*) **catarrhalis** is a common respiratory tract pathogen in man. The bacterium shows a strong tendency to form aggregates in vitro. A variant strain of *M. catarrhalis* that showed a reduced tendency to form aggregates was selected by successive in-vitro passage in broth culture from which aggregates had settled. The non-clumping variant strain showed alteration in expression of outer-membrane antigens, including the HMW-OMP, an outer-membrane protein of c. 200 kDa, outer-membrane protein CD and **lipo-oligosaccharide**. A mouse model for pulmonary challenge with *M. catarrhalis* revealed significant differences in the rate of clearance of the isogenic variant strains from the lung. The parent strain caused enhanced recruitment of neutrophils to the lung and more rapid clearance of bacteria from the lungs in comparison to the non-clumping variant. It is concluded that alteration of expression of surface molecules by *M. catarrhalis* has a significant impact in an in-vivo model of pulmonary clearance.

Searcher : Shears 308-4994

09/610034

L6 ANSWER 15 OF 35 MEDLINE DUPLICATE 8

ACCESSION NUMBER: 97296466 MEDLINE

DOCUMENT NUMBER: 97296466 PubMed ID: 9152030

TITLE: Moraxella (Branhamella) *catarrhalis*
--clinical and molecular aspects of a rediscovered pathogen.

AUTHOR: Enright M C; McKenzie H

CORPORATE SOURCE: Department of Biological Sciences, University of Sussex, Falmer, Brighton.

SOURCE: JOURNAL OF MEDICAL MICROBIOLOGY, (1997 May) 46 (5) 360-71. Ref: 129
Journal code: J2N; 0224131. ISSN: 0022-2615.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199705

ENTRY DATE: Entered STN: 19970609
Last Updated on STN: 19970609
Entered Medline: 19970529

AB Since its discovery at the end of the nineteenth century, Moraxella (Branhamella) *catarrhalis* has undergone several changes of nomenclature and periodic changes in its perceived status as either a commensal or a pathogen. Molecular analysis based on DNA hybridisation or 16S rDNA sequence comparisons has established its phylogenetic position as a member of the Moraxellaceae and shown that it is related more closely to Acinetobacter spp. than to the genus Neisseria in which it was placed formerly. However, confusion with phenotypically similar Neisseria spp. can occur in the routine diagnostic laboratory if appropriate identification tests are not performed. M. *catarrhalis* is now accepted as the third commonest pathogen of the respiratory tract after Streptococcus pneumoniae and Haemophilus influenzae. It is a significant cause of otitis media and sinusitis in children and of lower respiratory tract infections in adults, especially those with underlying chest disease. Nosocomial spread of infection, especially within respiratory wards, has been reported. Invasive infection is uncommon, but analysis of reports for England and Wales between 1992 and 1995 revealed 89 cases of M. *catarrhalis* bacteraemia, with the peak incidence in children aged 1-2 years. Carriage rates of M. *catarrhalis* are high in children and in the elderly, but its role as a commensal organism has probably been overstated in the past. Approximately 90% of strains are now beta-lactamase positive and, given that the first such strain was reported in 1976, this represents a dramatic increase in frequency over the last 20

years which has not been paralleled in any other species. The BRO-1 and BRO-2 beta-lactamase enzymes of *M. catarrhalis* are found in other Moraxellaceae, but are not related to beta-lactamases of any other species and their origin is therefore unknown. Molecular and typing studies have shown that the *M. catarrhalis* species is genetically heterogeneous and these methods have aided epidemiological investigation. Studies of factors that may be related to pathogenicity have shown the existence of three serotypes of lipooligosaccharide and the presence of fimbriae and a possible capsule. Some strains are serum-resistant, probably by virtue of interference with complement action, whilst transferrin- and lactoferrin-binding proteins enable the organism to obtain iron from its environment. An antibody response in humans to various *M. catarrhalis* antigens, including highly conserved outer-membrane proteins, has been demonstrated. Increased understanding of the organism's pathogenic properties and the host response to it may help to identify suitable vaccine targets or lead to other strategies to prevent infection. Whilst it remains, at present, the third most important respiratory pathogen, the impact of immunisation strategies for other organisms may change this position. The speed with which *M. catarrhalis* acquired beta-lactamase demonstrates the capacity of this organism to surprise us.

L6 ANSWER 16 OF 35 MEDLINE DUPLICATE 9
 ACCESSION NUMBER: 97395751 MEDLINE
 DOCUMENT NUMBER: 97395751 PubMed ID: 9251851
 TITLE: Experimental otitis media induced by nonviable
 Moraxella *catarrhalis* in the guinea pig
 model.
 AUTHOR: Sato K
 CORPORATE SOURCE: Department of Otolaryngology, Niigata University
 School of Medicine, Japan.
 SOURCE: AURIS, NASUS, LARYNX, (1997 Jul) 24 (3) 233-8.
 Journal code: 9FZ; 7708170. ISSN: 0385-8146.
 PUB. COUNTRY: Netherlands
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199710
 ENTRY DATE: Entered STN: 19971224
 Last Updated on STN: 19971224
 Entered Medline: 19971027

AB Moraxella *catarrhalis* is a normal resident of the human nasopharyngeal flora, but it is also isolated from middle ear fluid of acute otitis media and otitis media with effusion patients. To determine whether *M. catarrhalis* has direct pathogenicity in the middle ear, heat-killed *M. catarrhalis* was

inoculated into the middle ear bullae of guinea pigs, and the inflammatory response was investigated. Middle ear mucosal histopathology observed in *M. catarrhalis*-inoculated ears included subepithelial edema, capillary dilatation, thickening of lamina propria mucosa, inflammatory cell and erythrocyte infiltration into the lamina propria mucosa. Inflammatory cell numbers, lysozyme and myeloperoxidase concentrations in the middle ear washing suspensions of *M. catarrhalis*-inoculated ears were significantly higher than control ears throughout the experiment. Therefore, nonviable *M. catarrhalis* induced middle ear inflammation and mucoperiosteal histopathology, which might be caused by direct injury of the nonviable bacteria (e.g. lipooligosaccharide or outer membrane proteins) and metabolic products of inflammatory cells.

L6 ANSWER 17 OF 35 SCISEARCH COPYRIGHT 2001 ISI (R)
 ACCESSION NUMBER: 96:807878 SCISEARCH
 THE GENUINE ARTICLE: VQ253
 TITLE: SYNTHESIS OF OLIGOSACCHARIDE STRUCTURES FROM THE
 LIPOPOLYSACCHARIDE OF MORAXELLA-CATARRHALIS
 AUTHOR: EKELOF K; OSCARSON S (Reprint)
 CORPORATE SOURCE: UNIV STOCKHOLM, ARRHENIUS LAB, DEPT ORGAN CHEM,
 S-10691 STOCKHOLM, SWEDEN (Reprint); UNIV STOCKHOLM,
 ARRHENIUS LAB, DEPT ORGAN CHEM, S-10691 STOCKHOLM,
 SWEDEN
 COUNTRY OF AUTHOR: SWEDEN
 SOURCE: JOURNAL OF ORGANIC CHEMISTRY, (01 NOV 1996) Vol. 61,
 No. 22, pp. 7711-7718.
 ISSN: 0022-3263.
 DOCUMENT TYPE: Article; Journal
 FILE SEGMENT: PHYS; LIFE
 LANGUAGE: ENGLISH
 REFERENCE COUNT: 19

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The synthesis of the octasaccharide [p-(trifluoroacetamido)phenyl]ethyl 4-O-[2-O-(2-acetamido-2-deoxy-alpha-D-glucopyranosyl)-beta-D-glucopyranosyl]-6-O-[2-O-[4-O-(4-O-alpha-D-galactopyranosyl-beta-D-galactopyranosyl)-alpha-D-glucopyranosyl]-beta-D-glucopyranosyl]-3-O-beta-D-glucopyranosyl-alpha-D-glucopyranoside, representing the outer part of the lipooligosaccharide from *Moraxella catarrhalis* serotype A, is described, together with a hepta-, a hexa-, and a pentasaccharide, composing parts thereof with shorter oligosaccharide chains substituted in the g-position of the central 3,4,6-branched glucose moiety. The versatility of the use of thioglycosides in oligosaccharide synthesis is shown, since throughout the synthesis thioglycosides are used as glycosyl donor precursors, either directly in dimethyl(methylthio)sulfonium triflate (DMTST)-promoted

coupling reactions or after conversion to the corresponding glycosyl bromide in silver triflate-promoted couplings. The effects of different protecting groups, anomeric leaving groups, and solvents used in the various coupling reactions are often substantial, which necessitates the use of easily convertible intermediates.

L6 ANSWER 18 OF 35 SCISEARCH COPYRIGHT 2001 ISI (R)
 ACCESSION NUMBER: 96:367035 SCISEARCH
 THE GENUINE ARTICLE: UJ185
 TITLE: ANTIBODY-RESPONSE IN RABBITS TO SEROTYPE-SPECIFIC DETERMINANTS IN LIPOPOLYSACCHARIDES FROM MORAXELLA-CATARRHALIS
 AUTHOR: RAHMAN M (Reprint); HOLME T
 CORPORATE SOURCE: KAROLINSKA INST, MICROBIOL & TUMORBIOL CTR, S-17177 STOCKHOLM, SWEDEN (Reprint)
 COUNTRY OF AUTHOR: SWEDEN
 SOURCE: JOURNAL OF MEDICAL MICROBIOLOGY, (MAY 1996) Vol. 44, No. 5, pp. 348-354.
 ISSN: 0022-2615.
 DOCUMENT TYPE: Article; Journal
 FILE SEGMENT: LIFE
 LANGUAGE: ENGLISH
 REFERENCE COUNT: 25

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Antibodies against the serotype determinant epitopes of *Moraxella catarrhalis* lipopolysaccharides (LPS) were demonstrated in sera from rabbits immunised with whole bacterial cells. Purified LPS preparations from eight strains of *M. catarrhalis* were used as antigens in enzyme-linked immunosorbent assays (ELISA) and immunoblotting. The serotype specificity of the antibodies was shown by neutralisation with LPS and with purified polysaccharide obtained from LPS prepared from strains belonging to different serotypes. In immunoblots, antisera against the A and B LPS serotypes reacted only with LPS of its own type, confirming the presence of type-specific antibodies. A weak band was observed with type A LPS and antibody to type C, indicating cross-reactivity between the A and C serotypes. This cross-reaction can be explained on the basis of the known chemical structure of the LPS of the different serotypes. After heterologous absorption of sera, bands were obtained with homologous LPS antigen. These results suggest that the predominant antibody response in rabbits to LPS from *M. catarrhalis* is serotype-specific, unlike that previously observed in infected human patients.

L6 ANSWER 19 OF 35 SCISEARCH COPYRIGHT 2001 ISI (R)
 ACCESSION NUMBER: 96:831159 SCISEARCH
 THE GENUINE ARTICLE: VR778
 TITLE: MONOCLONAL-ANTIBODIES AGAINST HAEMOPHILUS-INFLUENZAE

LIPOPOLYSACCHARIDES - CLONE MAHI-4 BINDING TO A
PENTASACCHARIDE CONTAINING TERMINAL BETA-GAL
RESIDUES AND CLONE MAHI-10 RECOGNIZING TERMINAL
PHOSPHORYLATED SACCHARIDE RESIDUES

AUTHOR: BORRELLI S; JANSSON P E (Reprint); LINDBERG A A
CORPORATE SOURCE: KAROLINSKA INST, HUDDINGE HOSP, NOVUM, CLIN RES CTR,
S-14186 HUDDINGE, SWEDEN (Reprint); KAROLINSKA INST,
HUDDINGE HOSP, NOVUM, CLIN RES CTR, S-14186
HUDDINGE, SWEDEN
COUNTRY OF AUTHOR: SWEDEN
SOURCE: MICROBIAL PATHOGENESIS, (NOV 1996) Vol. 21, No. 5,
pp. 307-318.
ISSN: 0882-4010.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 25

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Mouse monoclonal antibodies MAHI 4 and MAHI 10 reactive with
Haemophilus influenzae lipopolysaccharide (LPS), were generated by
fusing mouse myeloma cells with spleen cells of mice immunized with
H. influenzae strain RM.7004-XP-1. The antibody MAHI 4 reacted in
whole-cell enzyme immunoassay (EIA) and colony-dot-immunoblotting
with 20 of 123 H. influenzae strains and to a few other human
Haemophilus spp. and Neisseria spp., but not to any Bordetella
pertussis, B. parapertussis, Aeromonas spp. or Moraxella
catarrhalis strains tested. This suggests a specific epitope
accessible to recognition in just a few strains. This conclusion was
supported by the data on binding of MAHI 4 to only three of 18 H.
influenzae LPSs tested, but not to any Haemophilus ducreyi or
enterobacterial LPSs. The antibody MAHI 10 bound to 80 of 123
strains of H. influenzae and to a few strains of Neisseria spp. and
M. **catarrhalis** as evaluated by EIA and
colony-dot-immunoblotting, which suggests an epitope accessible to
recognition in 65% of the H. influenzae strains tested. The antibody
MAHI 10 reacted with 10 of 18 H. influenzae LPSs as determined by
EIA. By using polysaccharides, obtained after both mild acidic
hydrolysis, strong alkali treatment, and dephosphorylation, as
inhibitors of the antibodies binding to N. influenzae LPS antigens
it was shown that phosphate groups were essential for the binding of
MAHI 10 to LPS but they did not affect antigenic recognition by MAHI
4. None of the monoclonal antibodies bound to isolated lipid A, but
the aggregation caused by the fatty acids of lipid A was essential
for optimum epitope recognition. Enzymatic treatment of homologous
LPSs with galactose-oxidase led to products which were between 20 to
30 times less effective as inhibitors of the binding of the MAHI 4
than the native LPSs. Taken together the results indicate that MAHI
4 has the following pentasaccharide as the epitope Gal beta 1-->2Hep

alpha 1-->2Hep alpha 1-->3Hep alpha 1-->Kdo(P). These results emphasize the importance of the terminal beta-Gal residue in the definition of the MAHI 4 specificity, and of the terminal phosphorlylated saccharide residues of some of the Haemophilus LPSs for the MAHI 10 specificity. (C) 1996 Academic Press Limited

L6 ANSWER 20 OF 35 MEDLINE DUPLICATE 10
 ACCESSION NUMBER: 96261755 MEDLINE
 DOCUMENT NUMBER: 96261755 PubMed ID: 8801433
 TITLE: Branhamella **catarrhalis**: epidemiology, surface antigenic structure, and immune response.
 AUTHOR: Murphy T F
 CORPORATE SOURCE: Department of Medicine, State University of New York at Buffalo, USA.. cammurph@ubvms.cc.buffalo.edu
 CONTRACT NUMBER: AI 28304 (NIAID)
 SOURCE: MICROBIOLOGICAL REVIEWS, (1996 Jun) 60 (2) 267-79.
 Ref: 186
 Journal code: M9M; 7806086. ISSN: 0146-0749.
 PUB. COUNTRY: United States
 Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, ACADEMIC)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199609
 ENTRY DATE: Entered STN: 19961015
 Last Updated on STN: 19961015
 Entered Medline: 19960930

AB Over the past decade, Branhamella **catarrhalis** has emerged as an important human pathogen. The bacterium is a common cause of otitis media in children and of lower respiratory tract infections in adults with chronic obstructive pulmonary disease. B. **catarrhalis** is exclusively a human pathogen. It colonizes the respiratory tract of a small proportion of adults and a larger proportion of children. Studies involving restriction enzyme analysis of genomic DNA show that colonization is a dynamic process, with the human host eliminating and acquiring new strains frequently. The surface of B. **catarrhalis** contains outer membrane proteins, lipooligosaccharide, and pili. The genes which encode ~~several outer membrane proteins~~ have been cloned, and some of these proteins are being studied as potential vaccine antigens. Analysis of the immune response has been limited by the lack of an adequate animal model of B. **catarrhalis** infection. New information regarding outer membrane structure should guide studies of the human immune response to B. **catarrhalis**. Immunoassays which specifically detect antibodies to determinants exposed on the bacterial surface will elucidate the most relevant immune response. The recognition of B. **catarrhalis** as an

important human pathogen has stimulated research on the epidemiology and surface structures of the bacterium. Future studies to understand the mechanisms of infection and to elucidate the human immune response to infection hold promise of developing new methods to treat and prevent infections caused by *B. catarrhalis*.

L6 ANSWER 21 OF 35 SCISEARCH COPYRIGHT 2001 ISI (R)
 ACCESSION NUMBER: 96:423141 SCISEARCH
 THE GENUINE ARTICLE: UP080
 TITLE: BRANHAMELLA-CATARRHALIS - EPIDEMIOLOGY,
 SURFACE ANTIGENIC STRUCTURE, AND IMMUNE-RESPONSE
 AUTHOR: MURPHY T F (Reprint)
 CORPORATE SOURCE: VET ADM MED CTR, MED RES 151, 3495 BAILEY AVE,
 BUFFALO, NY, 14215 (Reprint); STATE UNIVERSITY NEW
 YORK BUFFALO, DIV INFECT DIS, DEPT MED, BUFFALO, NY,
 00000; STATE UNIVERSITY NEW YORK BUFFALO, DIV INFECT
 DIS, DEPT MICROBIOL, BUFFALO, NY, 00000
 COUNTRY OF AUTHOR: USA
 SOURCE: MICROBIOLOGICAL REVIEWS, (JUN 1996) Vol. 60, No. 2,
 pp. 267.
 ISSN: 0146-0749.
 DOCUMENT TYPE: General Review; Journal
 FILE SEGMENT: LIFE
 LANGUAGE: ENGLISH
 REFERENCE COUNT: 187

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Over the past decade, *Branhamella catarrhalis* has emerged as an important human pathogen. The bacterium is a common cause of otitis media in children and of lower respiratory tract infections in adults with chronic obstructive pulmonary disease. *B. catarrhalis* is exclusively a human pathogen. It colonizes the respiratory tract of a small proportion of adults and a larger proportion of children. Studies involving restriction enzyme analysis of genomic DNA show that colonization is a dynamic process, with the human host eliminating and acquiring new strains frequently. The surface of *B. catarrhalis* contains outer membrane proteins, lipooligosaccharide, and pili. The genes which encode several outer membrane proteins have been cloned, and some of these proteins are being studied as potential vaccine antigens. Analysis of the immune response has been limited by the lack of an adequate animal model of *B. catarrhalis* infection. New information regarding outer membrane structure should guide studies of the human immune response to *B. catarrhalis*. Immunoassays which specifically detect antibodies to determinants exposed on the bacterial surface will elucidate the most relevant immune response. The recognition of *B. catarrhalis* as an important human pathogen has stimulated research on the epidemiology and surface structures of the bacterium. Future studies to

under-stand the mechanisms of infection and to elucidate the human immune response to infection hold promise of developing new methods to treat and prevent infections caused by *B. catarrhalis*.

L6 ANSWER 22 OF 35 MEDLINE DUPLICATE 11
 ACCESSION NUMBER: 96381129 MEDLINE
 DOCUMENT NUMBER: 96381129 PubMed ID: 8789142
 TITLE: Separation and characterization of O-deacylated lipooligosaccharides and glycans derived from *Moraxella catarrhalis* using capillary electrophoresis-electrospray mass spectrometry and tandem mass spectrometry.
 AUTHOR: Kelly J; Masoud H; Perry M B; Richards J C; Thibault P
 CORPORATE SOURCE: Department of Chemistry, Dalhousie University, Halifax, Nova Scotia, Canada.
 SOURCE: ANALYTICAL BIOCHEMISTRY, (1996 Jan 1) 233 (1) 15-30. Journal code: 4NK; 0370535. ISSN: 0003-2697.
 PUB. COUNTRY: United States
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199610
 ENTRY DATE: Entered STN: 19961106
 Last Updated on STN: 19961106
 Entered Medline: 19961021
 AB Electrophoretic methods have been developed for the analysis of complex carbohydrates derived from lipooligosaccharides (LOS) of *Moraxella catarrhalis* using capillary electrophoresis coupled to electrospray mass spectrometry (CE-ESMS). Separation of lipooligosaccharides (LOS) arising from mild hydrazinolysis of the intact lipopolysaccharides (LPS) was achieved using aqueous ammonium formate, and enabled identification of sites of heterogeneity (phosphates, phosphoethanolamine, and pendant acyl groups) on either the lipid A or the core oligosaccharide. More complex mixtures of carbohydrates obtained from the complete deacylation and dephosphorylation of LOS were amenable to electrophoretic conditions using both anionic and cationic separation. In particular, electrophoretic conditions were developed which permitted resolution of closely related oligosaccharides according to the number of carbohydrate residues appended to the core structure. Structural characterization of carbohydrates and LOS released from the hydrazinolysis and acid hydrolysis treatment of the intact LPS was achieved using tandem mass spectrometry (MS-MS) for samples introduced by direct flow injection. Taken together, the combination of CE-ESI-MS and MS-MS analyses provided valuable information on the heterogeneity of the LOS population in which a significant level of

variability was found mostly in the lipid A portion.

L6 ANSWER 23 OF 35 SCISEARCH COPYRIGHT 2001 ISI (R)
 ACCESSION NUMBER: 95:580127 SCISEARCH
 THE GENUINE ARTICLE: RQ792
 TITLE: THE TETRASACCHARIDE L-ALPHA-D-HEPTOSE1-]2-L-ALPHA-D-HEPTOSE1-]3-L-ALPHA-D-HEPTOSE1-] (3-DEOXY-D-MANNO-OCTULOSONIC ACID) AND PHOSPHATE IN LIPID-A DEFINE THE CONSERVED EPITOPE IN HAEMOPHILUS LIPOPOLYSACCHARIDES RECOGNIZED BY A MONOCLONAL-ANTIBODY
 AUTHOR: BORRELLI S; HEGEDUS O; SHAW D H; JANSSON P E (Reprint); LINDBERG A A
 CORPORATE SOURCE: HUDDINGE UNIV HOSP, KAROLINSKA INST, NOVUM, CLIN RES CTR, S-14186 HUDDINGE, SWEDEN (Reprint); HUDDINGE UNIV HOSP, KAROLINSKA INST, NOVUM, CLIN RES CTR, S-14186 HUDDINGE, SWEDEN; KAROLINSKA INST, DEPT IMMUNOL MICROBIOL PATHOL & INFECT DIS, DIV CLIN BACTERIOL, S-14186 HUDDINGE, SWEDEN; FISHERIES & OCEANS CANADA, SCI BRANCH, ST JOHNS, NF A1C 5X1, CANADA
 COUNTRY OF AUTHOR: SWEDEN; CANADA
 SOURCE: INFECTION AND IMMUNITY, (SEP 1995) Vol. 63, No. 9, pp. 3683-3692.
 ISSN: 0019-9567.
 DOCUMENT TYPE: Article; Journal
 FILE SEGMENT: LIFE
 LANGUAGE: ENGLISH
 REFERENCE COUNT: 56

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A murine monoclonal antibody, MAHI 3 (immunoglobulin G2b), that is broadly reactive with Haemophilus influenzae lipopolysaccharides (LPSs) but nonreactive with all enterobacterial LPSs tested was generated by fusing mouse myeloma cells with spleen cells of BALB/c mice immunized with azide-killed H. influenzae RM.7004. MAHI 3 bound to all H. influenzae, all other human Haemophilus spp., all Bordetella pertussis and Bordetella parapertussis, and all Aeromonas spp. tested but not to any Neisseria or Moraxella catarrhalis strains, as determined by enzyme immunoassay, colony dot immunoblotting, and immunoblotting. In an inhibition enzyme immunoassay, MAHI 3 reacted with all 45 H. influenzae LPSs tested but not with the LPS from the rough mutant 169 Rd(-)/b(+), which has only 3-deoxy-D-manno-octulosonic acid (P) [Kdo(P)] and lipid A. The antibody was not inhibited by H. influenzae lipid A or lipid-free polysaccharide isolated after mild acid hydrolysis. Only native LPSs show positive inhibitory activity, indicating that part of lipid A is involved in the binding of MAHI 3. From the results, it is indicated that the structural element recognized by MAHI 3 is

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Hep alpha 1-->2Hep alpha 1-->3Hep alpha 1-->Kdo together with part of lipid A, including the phosphate.

L6 ANSWER 24 OF 35 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 95211773 MEDLINE
DOCUMENT NUMBER: 95211773 PubMed ID: 7535189
TITLE: Structural studies of the O-antigen oligosaccharides from two strains of *Moraxella catarrhalis* serotype C.
AUTHOR: Edebrink P; Jansson P E; Rahman M M; Widmalm G; Holme T; Rahman M
CORPORATE SOURCE: Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, Sweden.
SOURCE: CARBOHYDRATE RESEARCH, (1995 Jan 17) 266 (2) 237-61. Journal code: CNY; 0043535. ISSN: 0008-6215.
PUB. COUNTRY: Netherlands
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950510
Last Updated on STN: 19960129
Entered Medline: 19950504

AB The oligosaccharide parts from *Moraxella* (*Branhamella*) *catarrhalis* serotype C lipooligosaccharides were isolated by mild acid hydrolysis followed by gel permeation chromatography. Four different oligosaccharides could be identified from strain RS26 and two from strain RS10. The structures of the O-oligosaccharides were established by methylation analyses, mass spectrometry, and NMR spectroscopy. It is concluded that the oligosaccharide O-antigens from RS26 are a mixture of octa-, deca-, and undeca-saccharides, and most likely a heptasaccharide. Strain RS10 contains the deca- and the undeca-saccharide only. The structures for the oligosaccharides are shown below. [formula: see text] OS(7) [formula: see text] OS(8) [formula: see text] OS(10) [formula: see text] OS(11) Methylation analysis of the intact lipooligosaccharides showed that two Kdo residues were present, one terminal and one 4,5-substituted residue. It also showed that they consisted of a lipid A portion with 6-substituted glucosamine residues.

L6 ANSWER 25 OF 35 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 95:778471 SCISEARCH
THE GENUINE ARTICLE: TD377
TITLE: BINDING-SPECIFICITY FOR 4 MONOCLONAL-ANTIBODIES RECOGNIZING TERMINAL GAL-ALPHA-1-]4GAL RESIDUES IN HAEMOPHILUS-INFLUENZAE LIPOPOLYSACCHARIDE
AUTHOR: BORRELLI S; ALTMANN K; JANSSON P E (Reprint);

Searcher : Shears 308-4994

LINDBERG A A

CORPORATE SOURCE: HUDDINGE HOSP, NOVUM, KAROLINSKA INST, CLIN RES CTR, S-14186 HUDDINGE, SWEDEN (Reprint); HUDDINGE HOSP, NOVUM, KAROLINSKA INST, CLIN RES CTR, S-14186 HUDDINGE, SWEDEN; HUDDINGE HOSP, NOVUM, KAROLINSKA INST, DEPT IMMUNOL MICROBIOL PATHOL & INFECT DIS, S-14186 HUDDINGE, SWEDEN.

COUNTRY OF AUTHOR: SWEDEN

SOURCE: MICROBIAL PATHOGENESIS, (SEP 1995) Vol. 19, No. 3, pp. 139-157.
ISSN: 0882-4010.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: ENGLISH

REFERENCE COUNT: 46

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Four murine monoclonal antibodies (MAbs) reactive with the outer-core region of the lipopolysaccharide (LPS) from *Haemophilus influenzae* were generated after immunization with azide-killed *H. influenzae* RM.7004 AH1-2 and their epitope specificities studied. The monoclonal antibodies: MAHI 6 (IgM), MAHI 5 (IgG2a), MAHI 8 (IgG3), and MAHI 11 (IgG2b) bound to synthetic glycoconjugates or glycolipids with terminal galabiosyl (Gal alpha 1 --> 4Gal beta 1-) or globotriaosyl (Gal alpha 1 --> 4Gal beta 1 1 --> 4GLc) residues as evaluated in enzyme immunoassays (EIA). Glycoconjugates or glycolipids with internally placed galabiose elements were not active, indicating selectivity of the MAbs for recognition of the epitope. Nine LPSs from *H. influenzae* inhibited the binding of the four MAbs. The presence of the galabiosyl disaccharide element in these nine LPSs was evidenced by the binding of I-125-labeled Shiga toxin isolated from the bacterium *Shigella dysenteriae* type 1, reported to have as receptor the Gal alpha 1 --> 4Gal beta disaccharide (Lindberg et al., *J Biol Chem*, 1987, 262: 1779-85). Structural studies of these *H. influenzae* LPSs were also in accord with the presence of the galabiosyl disaccharide, in addition H-1-NMR spectroscopy showed the presence of O-acetyl groups in the RM.7004 AH1-2 LPS. However, differential binding specificities of the MAbs to modified RM.7004 AH1-2 LPSs were observed. MAHI 6 and MAHI 11 bound equally well to LPS, polysaccharides obtained after mild acidic treatment, and dephosphorylated LPS samples as shown in inhibition EIA. In contrast, both dephosphorylated LPS samples and polysaccharides were poorer inhibitors of the binding of MAHI 5 and MAHI 8 to native RM.7004 AH1-2 LPS. Neither the de-O-acylated nor the de-O,N-acylated LPSs were effective inhibitors of any of the four MAbs. These results suggest that the MAbs recognition involves Gal alpha 1 --> 4Gal and O-acetyl and other saccharide residue(s) from the oligosaccharide moiety of the LPS. The epitopes are also expressed and accessible to recognition in clinical isolates coming

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from different sources of *Neisseria* spp., *Haemophilus* spp., and *Moraxella catarrhalis*, but not in *Bordetella* spp., *Aeromonas* spp. or Enterobacteriaceae as evaluated by whole-bacteria EIA and colony-dot-immunoblotting. (C) 1995 Academic Press Limited

L6 ANSWER 26 OF 35 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94196523 EMBASE
DOCUMENT NUMBER: 1994196523
TITLE: Isolation and characterization of lipopolysaccharides, lipooligosaccharides, and lipid A.
AUTHOR: Apicella M.A.; Griffiss J.M.; Schneider H.
CORPORATE SOURCE: Department of Microbiology, Iowa University College of Medicine, Iowa City, IA 52242, United States
SOURCE: Methods in Enzymology, (1994) 235/- (242-252).
ISSN: 0076-6879 CODEN: MENZAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English

L6 ANSWER 27 OF 35 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 93329207 MEDLINE
DOCUMENT NUMBER: 93329207 PubMed ID: 8335988
TITLE: Effect of immunization of pulmonary clearance of *Moraxella catarrhalis* in an animal model.
AUTHOR: Masiver I; Unhanand M; McCracken G H Jr; Hansen E J
CORPORATE SOURCE: Dept. of Microbiology, University of Texas Southwestern Medical Center, Dallas 75235-9048.
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (1993 Aug) 168 (2) 469-72.
Journal code: IH3; 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 19930903
~~Last Updated on STN: 19970203~~
~~Entered Medline: 19930824~~

AB A murine model for pulmonary clearance of *Moraxella catarrhalis* was used to determine whether immunization could enhance clearance of this organism from the lungs. Animals actively immunized with outer membrane vesicles of *M. catarrhalis* cleared an endobronchial challenge with the homologous strain more quickly than did sham-immunized control animals. Western blot analysis of both this immune mouse serum and rabbit antiserum raised against outer membrane vesicles of *M. catarrhalis*

indicated that antibodies were present to both outer membrane protein and lipooligosaccharide antigens. Passive immunization of mice with the immune rabbit serum resulted in enhanced pulmonary clearance of both homologous and heterologous strains of *M. catarrhalis*, indicating the involvement of serum antibody in this clearance process and the existence of conserved surface antigens in the two different *M. catarrhalis* strains. These results suggest that this model system may be useful for the identification of vaccine candidates among the surface antigens of *M. catarrhalis*.

L6 ANSWER 28 OF 35 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1993:410138 BIOSIS

DOCUMENT NUMBER: PREV199396075863

TITLE: Recombinant interferon-gamma enhances resistance to acute disseminated *Candida albicans* infection in mice.

AUTHOR(S): Kullberg, Bart-Jan; Van't Wout, Jan W.; Hoogstraten, Connie; Van Furth, Ralph (1)

CORPORATE SOURCE: (1) Dep. Infectious Diseases, Building 1 C5P, P.O. Box 9600, 2300 RC Leiden Netherlands Antilles

SOURCE: Journal of Infectious Diseases, (1993) Vol. 168, No. 2, pp. 436-443.
ISSN: 0022-1899.

DOCUMENT TYPE: Article

LANGUAGE: English

AB The effect of recombinant rat interferon-gamma (rIFN-gamma) on acute disseminated *Candida albicans* infection in mice was investigated. Outgrowth of *C. albicans* in kidneys, spleen, and liver of mice treated with one intravenous (iv) dose of rIFN-gamma before iv injection of 5 times 10⁵ cfu of *C. albicans* was significantly lower than in controls over 7 days. rIFN-gamma was protective when given 1 day before, simultaneously with, or 1-3 days after infection but not when given 3 days before. In mice pretreated with hydrocortisone acetate, rIFN-gamma significantly reduced the outgrowth only when 10³ cfu of *C. albicans* was injected. Injection of rIFN-gamma did not reduce the outgrowth of *C. albicans* in cyclophosphamide-pretreated mice and significantly increased the capacity of peripheral blood and exudate peritoneal granulocytes to kill *C. albicans* in vitro. Thus, rIFN-gamma enhances host resistance against acute disseminated *C. albicans* infection in mice through activation of polymorphonuclear leukocytes.

L6 ANSWER 29 OF 35 MEDLINE

DUPLICATE 14

ACCESSION NUMBER: 92307942 MEDLINE

DOCUMENT NUMBER: 92307942 PubMed ID: 1612771

TITLE: Further antigenic similarities of *Neisseria gonorrhoeae* lipooligosaccharides and human

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glycosphingolipids.
AUTHOR: Mandrell R E
CORPORATE SOURCE: Centre for Immunochemistry, Veterans Administration
Medical Center, San Francisco, California 94121.
CONTRACT NUMBER: AI21620 (NIAID)
AI24616 (NIAID)
SOURCE: INFECTION AND IMMUNITY, (1992 Jul) 60 (7) 3017-20.
Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199207
ENTRY DATE: Entered STN: 19920807
Last Updated on STN: 19920807
Entered Medline: 19920724
AB Anticarbhydrate monoclonal antibodies were tested for their ability
to bind to various strains of Neisseria. A monoclonal antibody that
binds to the ganglio-series glycosphingolipid, ganglio-N-
triaosylceramide, also bound to strains of Neisseria gonorrhoeae but
not to other species of Neisseria. An antibody specific for the
globo-series glycosphingolipid, globotriaosylceramide, also bound to
strains of N. gonorrhoeae, Neisseria meningitidis, Neisseria
lactamica, and Branhamella **catarrhalis** but not to any
other strains of nonpathogenic Neisseria.

L6 ANSWER 30 OF 35 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 93056822 MEDLINE
DOCUMENT NUMBER: 93056822 PubMed ID: 1431352
TITLE: Biochemical analysis of lipopolysaccharides from
respiratory pathogenic Branhamella
catarrhalis strains and the role of anti-LPS
antibodies in Branhamella respiratory infections.
AUTHOR: Tanaka H; Oishi K; Sonoda F; Iwagaki A; Nagatake T;
Matsumoto K
CORPORATE SOURCE: Department of Internal Medicine, Nagasaki University.
SOURCE: KANSENSHOGAKU ZASSHI. JOURNAL OF THE JAPANESE
ASSOCIATION FOR INFECTIOUS DISEASES, (1992 Jun) 66
(6) 709-15.
Journal code: IJR; 0236671. ISSN: 0387-5911.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921204

Searcher : Shears 308-4994

AB We characterized lipopolysaccharides (LPSs) from respiratory pathogenic *Branhamella catarrhalis* (BC) strains, and evaluated the protective property of anti-BC LPS antibody in BC respiratory infections. LPSs from four strains of BC were **lipooligosaccharide** having no O-side chain and a M(r) of 3 KDa, as estimated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE). All of them produced different patterns, showing two to four bands on SDS-PAGE. We found high level of anti-BC IgG antibody in convalescent sera from a patient with BC respiratory tract infection by ELISA. This IgG antibody recognized BC LPSs on Western blots. Two respiratory pathogens of BC (strains; 87-122, 88-23) were tested in a bactericidal assay employing a convalescent sera. 87-122 strain was susceptible to antibody-dependent, complement-mediated killing, while 88-23 strain was resistant. The killing of 87-122 strain was inhibited by addition of the homologous BC LPS to the convalescent sera in a dose-dependent manner. These data support that anti-BC LPS antibody may mediate complement-lysis of some strains of BC, and play a protective role in BC respiratory infections.

L6 ANSWER 31 OF 35 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1992:380719 BIOSIS

DOCUMENT NUMBER: BR43:47669

TITLE: IDENTIFICATION AND PURIFICATION OF THE
LIPOOLIGOSACCHARIDE-ASSOCIATED HIGH MOLECULAR
WEIGHT OUTER MEMBRANE PROTEIN HMW-OMP OF *BRANHAMELLA*-
CATARRHALIS.

AUTHOR(S): KLINGMAN K L; MURPHY T F

CORPORATE SOURCE: STATE UNIV. N.Y. BUFFALO, BUFFALO, N.Y.

SOURCE: 92ND GENERAL MEETING OF THE AMERICAN SOCIETY FOR
MICROBIOLOGY, NEW ORLEANS, LOUISIANA, USA, MAY 26-30,
1992. ABSTR GEN MEET AM SOC MICROBIOL, (1992) 92 (0),
90.

CODEN: AGMME8.

DOCUMENT TYPE: Conference

FILE SEGMENT: BR; OLD

LANGUAGE: English

L6 ANSWER 32 OF 35 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1992:380656 BIOSIS

DOCUMENT NUMBER: BR43:47606

TITLE: IMMUNE ENHANCEMENT OF PULMONARY CLEARANCE OF
MORAXELLA-*CATARRHALIS*.

AUTHOR(S): MACIVER I; UNHANAND M; HELMINEN M; MCCracken G H JR;
HANSEN E J

CORPORATE SOURCE: UNIV. TEXAS SOUTHWESTERN MED. CENTER, DALLAS, TEX.

SOURCE: 92ND GENERAL MEETING OF THE AMERICAN SOCIETY FOR
MICROBIOLOGY, NEW ORLEANS, LOUISIANA, USA, MAY 26-30,

1992. ABSTR GEN MEET AM SOC MICROBIOL, (1992) 92 (0),
80.

CODEN: AGMME8.

DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

L6 ANSWER 33 OF 35 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 91014645 MEDLINE
DOCUMENT NUMBER: 91014645 PubMed ID: 1699109
TITLE: **Lipooligosaccharide** epitopes shared among
gram-negative non-enteric mucosal pathogens.
AUTHOR: Campagnari A A; Spinola S M; Lesse A J; Kwaik Y A;
Mandrell R E; Apicella M A
CORPORATE SOURCE: Department of Medicine, State University of New York,
Buffalo 14215.
CONTRACT NUMBER: AI 18384 (NIAID)
AI 21620 (NIAID)
AI 24616 (NIAID)
+
SOURCE: MICROBIAL PATHOGENESIS, (1990 May) 8 (5) 353-62.
~~Journal code: MIC; 8606191. ISSN: 0882-4010.~~
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199010
ENTRY DATE: Entered STN: 19910117
~~Last Updated on STN: 19960129~~
Entered Medline: 19901027

AB The non-enteric Gram-negative human pathogens, *B. catarrhalis*, *H. ducreyi*, *H. influenzae*, *N. gonorrhoeae* and *N. meningitidis*, do not have repeating O-antigens as part of their principle surface glycolipid, the **lipooligosaccharide** (LOS). Because they have similar LOS structures, we studied the conservation of LOS oligosaccharide epitopes among these organisms. Twenty-one monoclonal antibodies (mAbs) generated by immunizing mice with *H. influenzae*, *N. gonorrhoeae* and *N. meningitidis* were studied for cross reactivity. Five mAbs generated against non-typable *H. influenzae* were the only strain-specific antibodies. Ten mAbs reacted to LOS epitope(s) common to a genera or species, and six mAbs bound to epitope(s) on the LOS of strains from different genera. Some cross reactive mAbs bound to LOS bands of similar molecular weights, while others bound to bands of varying molecular weights. mAb 3F11, whose epitope mimics a human blood-group antigen, bound to a 4.8 kDa LOS band in *N. gonorrhoeae* and *H. ducreyi*, two pathogens that infect genital epithelium. mAb 3D9,

whose epitope consists of 2-keto-3-deoxyoctulosonic acid (KDO), reacted with different LOS bands in *N. gonorrhoeae*, *H. influenzae* and some R mutants of *S. minnesota*. A 14 kb restriction fragment containing **lipooligosaccharide** synthesis genes responsible for the assembly of the 3D9 epitope in *H. influenzae* hybridized to all *H. influenzae* strains tested but did not hybridize to gonococcal and *S. minnesota* strains that expressed this epitope. These studies demonstrate that conserved LOS epitope(s) exist among different species and genera of non-enteric human pathogens and that different genetic mechanisms may have evolved in these pathogens to assemble some of these conserved epitopes.

L6 ANSWER 34 OF 35 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1989:314362 BIOSIS

DOCUMENT NUMBER: BA88:28092

TITLE: ISOLATION OF THE OUTER MEMBRANE OF *BRANHAMELLA-CATARRHALIS*.

AUTHOR(S): MURPHY T F; LOEB M R

CORPORATE SOURCE: DIV. INFECTIOUS DIS., ERIE COUNTY MED. CENT, 462 GRIDER ST., BUFFALO, N.Y. 14215.

SOURCE: MICROB PATHOG, (1989) 6 (3), 159-174.
CODEN: MIPAEV. ISSN: 0882-4010.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB The emergence of *Branhamella catarrhalis* as an important human pathogen has stimulated interest in investigation of the outer membrane (OM) of the bacterium. In this study, the OM of *B. catarrhalis* was isolated and partially characterized. Radiolabelled cells were lysed and fractionated by isopycnic centrifugation in a continuous sucrose gradient. Five fractions were identified. Fraction A consisted of OM fragments of varying density. Fractions B and C were OM of a discrete density containing some cytoplasmic membrane. Fraction D was cytoplasmic membrane and Fraction E contained smaller less dense fragments of cytoplasmic membrane. The protein composition of the *Branhamella* OM is typical for that of Gram-negative bacteria in that approximately 10 to 20 proteins were present with six to eight of these proteins predominating. Having isolated and partially characterized the OM by sucrose density centrifugation, five simpler techniques for isolating OM were employed and the preparations compared to OM isolated on the gradient. Techniques that are based on differential detergent solubility of OM and cytoplasmic membranes were ineffective in isolating OM of *B. catarrhalis*. By contrast techniques that involved collection of OM vesicles were successful in isolating OM of *B. catarrhalis*. collection of vesicles from broth culture supernatants and EDTA-heat-induced vesicles were identified as convenient and reliable methods for isolating OM. Isolating and partially characterizing the OM of *B. catarrhalis*

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represents an initial step in a systematic study of outer membrane antigens of the bacterium.

L6 ANSWER 35 OF 35 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1989:198079 BIOSIS
DOCUMENT NUMBER: BR36:98528
TITLE: THE SURFACE OF BRANHAMELLA-CATARRHALIS A
SYSTEMATIC APPROACH TO THE SURFACE ANTIGENS OF AN
EMERGING PATHOGEN.
AUTHOR(S): MURPHY T F
CORPORATE SOURCE: DIV. INFECTIOUS DISEASES, ERIE COUNTY MED. CENT., 462
GRIDER ST., BUFFALO, N.Y. 14215.
SOURCE: WORKSHOP ON VACCINES FOR OTITIS MEDIA, PITTSBURGH,
PENNSYLVANIA, USA, SEPTEMBER 1-2, 1988. PEDIATR
INFECT DIS, (1988) 8 (1 SUPPL), S75-S77.
CODEN: PIDJEV.
FILE SEGMENT: BR; OLD
LANGUAGE: English

FILE 'HOME' ENTERED AT 11:53:41 ON 25 JUL 2001